VOLUME 84 NUMBER 2

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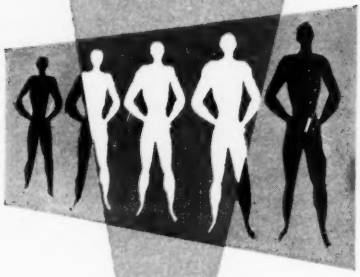

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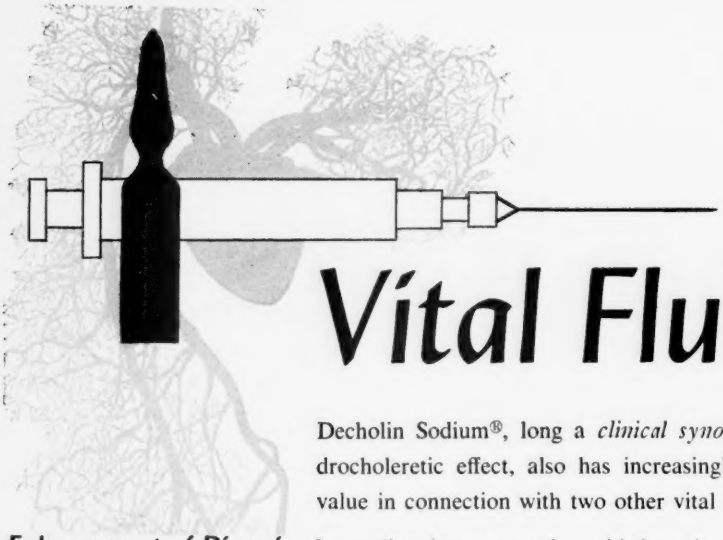

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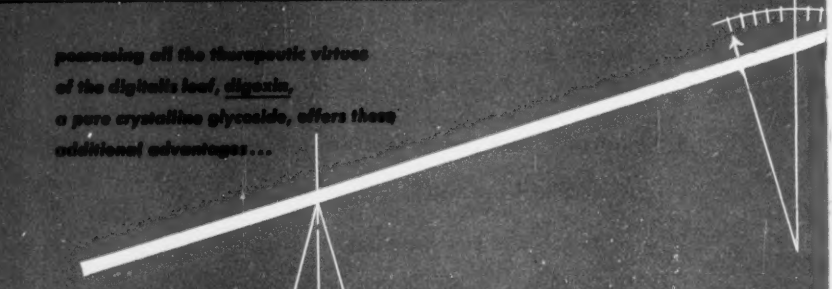

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1 Philpott, N. W., Hendelman, M., and Primrose, T.: Methionine in Obstetrics, Am. Jr. Obst. & Gynec. 57:125–142 Jan. 1949.

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1. Brewster, J. M., U. S. Naval Med. Bull. **49**: 1-11, January-February 1949.

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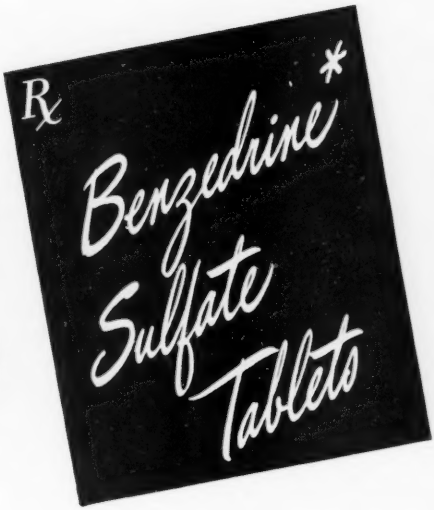

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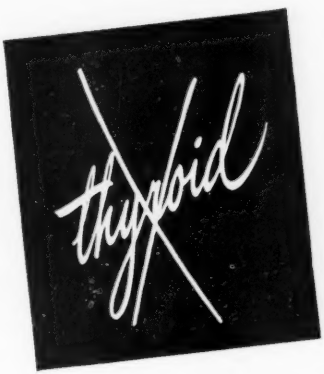
Rynearson, E. H., and Gastineau, C. F.: Obesity, Springfield, Charles C. Thomas, 1949, p. 94



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BIBLIOGRAPHY: (1) Modell, W.; Gold, H., and Clarke, D. A.: J. Pharmacol. & Exper. Therap. **84**:284, 1945. (2) Gold, H., and others: Am. J. Med. **3**:665, 1947. (3) New and Nonofficial Remedies, Philadelphia, J. B. Lippincott Co., 1947, p. 298. (4) Finkelstein, M. B., and Smyth, C. J.: J. Mich. State M. Soc. **45**:1618, 1946. (5) Reaser, P. B., and Burch, G. E.: Proc. Soc. Exper. Biol. & Med. **63**:543, 1946. (6) Griggs, D. E., and Johns, V. J.: Influence of mercurial diuretics on sodium excretion, to be published.

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ARCHIVES of INTERNAL MEDICINE

VOLUME 84 AUGUST 1949 NUMBER 2

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GASTROSCOPIC AND HISTOLOGIC APPEARANCE OF THE GASTRIC MUCOSA BEFORE AND AFTER VAGOTOMY FOR PEPTIC ULCER

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ELEANOR M. HUMPHREYS, M.D.

LESTER R. DRAGSTEDT, M.D.

AND

WALTER LINCOLN PALMER, M.D.

CHICAGO

THE PURPOSE of this paper is to describe the appearance of the gastric mucosa before and after vagotomy. A total of 125 gastroscopies were performed on 27 patients, 26 of whom had peptic ulcer and 1 of whom had a functional gastrointestinal disturbance; 18 were examined before and after operation and 9 after vagotomy only. The criteria for the diagnosis of gastritis were essentially those formulated by Schindler.[1] The stomach also was examined histologically in 11 patients, in 3 at the time of resection of a gastric ulcer, developing approximately five months to four years after vagotomy, and in 8 at autopsy, performed from one week to two years and three months after operation.

Wolff [2] examined gastroscopically 8 patients with duodenal ulcer and 3 with gastric ulcer, one week to eleven months after vagotomy, and observed a dull and reddened mucosa in 7 and a normal mucosa in 4. Gastric tonus was diminished; retention of food, blunting of the angulus and obliteration of the musculosphincter of the antrum were noted. The last two changes disappeared temporarily in the 3 patients given urecholine® (carbaminoyl-beta-methylcholine chloride) subcutaneously. The gastric ulcers healed promptly. Wolf and Andrus [3] noted pallor of the mucosa after vagotomy in a patient with gastrostomy. Spontaneous motor activity was absent, but mild hyperemia and engorgement were

From the Frank Billings Medical Clinic, Department of Medicine, and the Departments of Pathology and Surgery, University of Chicago.

1. Schindler, R.: Gastritis, New York, Grune & Stratton, Inc., 1947.

2. Wolff, R.: The Gastroscopic Appearance of the Gastric Mucosa Before and After Vagotomy, Gastroenterology **10**:231, 1948.

3. Wolf, S., and Andrus, W. D.: The Effect of Vagotomy on Gastric Function, Gastroenterology **8**:429, 1947.

observed after the ingestion of a meal; the injection of neostigmine methylsulfate U. S. P. produced hyperemia, though it was less pronounced than before vagotomy.

Paulson and Gladsden [4] observed no alterations in the appearance of the gastric mucosa in patients with vagotomy alone; however, peristaltic activity was decreased. In persons with vagotomy and gastroenterostomy "some negligible mucosal changes" were sometimes present. In patients with vagotomy and partial gastric resection, the edema, thickening and nodular hypertrophy, with or without erythema and friability, were regarded as similar to those changes noted in the absence of vagotomy.

Asher [5] performed gastroscopy in 20 cases, 19 of duodenal ulcer and 1 of a jejunal ulcer, at intervals of from three to twelve months after vagotomy, alone or combined with pyloroplasty or gastroenterostomy. Of the 8 cases in which vagotomy alone was done, preoperative examination was made in 4; superficial changes were noted in 2, hypertrophic changes in 1 and a normal mucosa in 1. A postoperative diagnosis of superficial or hypertrophic gastritis, with or without erosions, was made in 6 cases, of erosions alone in 1 case and of a normal mucosa in 1 case. Normal motility was recorded in 5 cases of this group; spasm and atony were noted in 1 case each, and atony and spasm in 1 case, on separate examinations. Of the 12 cases in which vagotomy and gastroenterostomy or pyloroplasty was performed, a preoperative examination had been made in 7; a diagnosis of normal mucosa had been made in 2, of superficial gastritis in 4 and of a severe, mixed type of stomal gastritis in 1. After operation, superficial or hypertrophic inflammation, with or without erosions, was noted in 7 cases, atrophy in 1 and a normal mucosa in 3; an erosion was observed in 1 case three months after vagotomy, but the mucosa appeared normal three months later. Normal motility was seen in 1 case, spasm in 5, decreased motility in 1 and atony in 4; in 1 case spasm was noted three months after vagotomy, but motility appeared normal gastroscopically three months later.

GASTROSCOPIC OBSERVATIONS BEFORE AND AFTER VAGOTOMY

Duodenal Ulcer.—The data on the 14 patients with duodenal ulcer and the 3 patients with both duodenal and gastric ulcer are summarized in table 1. Gastric retention was present in 5 of the 6 patients treated with vagotomy alone; the retention was temporary in the 2 patients of this group who were examined more than once. Retention was not

4. Paulson, M., and Gladsden, E. S.: Medical Aspects of Vagotomy for Peptic Ulcer, Bull. Johns Hopkins Hosp. **81**:107, 1947.

5. Asher, L. M.: The Gastric Mucosa After Vagotomy for Peptic Ulcer: A Gastroscopic Study, Gastroenterology **11**:303, 1948.

observed gastroscopically in 10 of the 11 patients in whom a gastroenterostomy had been established prior to, or concomitantly with, the vagotomy. The appearance of the mucosa had not changed significantly in 9 of the 11 patients examined before and after operation; 5 originally presented a normal mucosa and 4 gastritis. The stomach appeared essentially normal after vagotomy in 2 patients for whom a diagnosis of moderate hypertrophic gastritis and superficial inflammation, respectively, had been made before operation. Gastroscopy was not performed before operation on 6 patients (cases 10, 11, 12, 13, 14 and 17); 3 of these presented a normal mucosa two, five and one-half and thirty months, respectively, after vagotomy. A moderate superficial gastritis was observed in 1 patient twelve months after vagotomy and gastroenterostomy. Superficial changes and a normal mucosa were observed at various examinations in another patient, during a postoperative period of twenty-six months. The superficial gastritis in the sixth patient, which appeared three years after vagotomy, may possibly have been related to the previously administered irradiation of the stomach. Rapid healing was observed in 2 of the 3 patients with concomitant gastric ulcer.

The insulin test for the integrity of vagal innervation, performed after operation on 12 patients, yielded negative results; a positive acid response was elicited in 1 patient (case 3) several months later. (The reliability of the insulin test as an indicator of complete or incomplete vagotomy has not been fully evaluated.) Gastric ulcers developed after vagotomy in 2 patients (cases 4 and 13); these cases, therefore, are described in more detail.

CASE 4.—W. B., a 63 year old man with a duodenal ulcer of eight years' duration, had received a total of 1,260 r (depth dose) in divided amounts to the fundus and body of the stomach, for the purpose of reducing gastric acidity. The maximum free hydrochloric acid (histamine test) decreased temporarily from a range of 108 to 116 clinical units to 60, but returned subsequently to original levels; in the ensuing four years the amount of acidity fluctuated between 108 and 126 clinical units. Three gastroscopies during this period demonstrated, at various times, minimal superficial inflammation, pigmented areas and mild, localized, hypertrophic gastritis. The mucosa, fourteen months after transthoracic vagotomy, appeared normal; shallow peristaltic waves were observed in the antrum. Ulcer distress recurred four years and three months after operation; roentgenoscopy then disclosed a huge ulcer crater on the lesser curvature of the stomach. Gastroscopy demonstrated a large, benign ulcer on the anterior wall of the lesser curvature of the stomach, immediately above the angulus. The mucosa adjacent to the ulcer was reddened, edematous and hemorrhagic, but elsewhere it appeared normal. Peristaltic activity was vigorous. Free acid was present in the gastric content; the exact amount was not recorded. The result of the insulin test was negative. At operation, an intact vagus fiber was identified within the muscle layer on the posterior wall of the esophagus, and severed; a partial gastric resection was performed, with the removal of a benign ulcer. The microscopic appearance of the stomach is described later in this paper.

TABLE 1.—*Gastroscopic Appearance of Gastric Mucosa Before and After Vagotomy in 17 Patients with Duodenal Ulcer*

		Before Vagotomy				After Vagotomy			Gastroscopic Observations	
Case	Sex and Age	No. of Examinations	Interval Before Operation	Gastric Mucosa	Type of Vagotomy	No. of Examinations	Postoperative Interval	Gastric Mucosa	Peristalsis	Gastric Retention
Patients with Duodenal Ulcer, no Previous Operation, Vagotomy										
1 S. R.	M 48	1	4 days	Normal	Thoracic	1	3½ mo.	Normal	Shallow	+
2 R. P.	M 58	1	7 days	Essentially normal	Abdominal	1	3 mo.	Normal	Moderate	+
3 L. H.	M 42	1	2 days	Moderate, superficial gastritis of the antrum	Abdominal	1	4 mo.	Normal	Moderate	Slight
4 W. B.	M 63	3	4 yr.	Mild, superficial gastritis; hemorrhages; localized, hypertrophic gastritis	Thoracic	2	14 mo. 4¾ yr.	Normal Gastric ulcer above angulus; adjacent mucosa, edematous and hemorrhagic; elsewhere, normal	Shallow Active	+ —
Patients with Duodenal Ulcer, Previous Gastroenterostomy, Vagotomy										
5 N. R.	M 35	1	2½ mo.	Moderate hypertrophic gastritis	Abdominal	1	6 wk.	Gastric mucosa normal; hyperemia and edema at stoma	Present	—
6 A. V.	M 48	1	7 days	Normal	Abdominal	1	9 mo.	Normal	Present	—
7 M. L.	F 50	2	9 yr., 8 mo. 3 days	Mild, localized, superficial gastritis Normal; mild edema at stoma	Abdominal	1	4 mo.	Normal	Present	—
Patients with Duodenal Ulcer, no Previous Operation, Vagotomy and Later Gastroenterostomy										
8 D. O'N.	M 65	1	2 days	Moderate, hemorrhagic hypertrophic gastritis	Abdominal	1	3 mo.	Mild hypertrophic gastritis; prominent rugae	Active	—
9 C. L.	M 40	1	3 days	Moderate hemorrhagic gastritis; adherent mucus; prominent rugae	Abdominal	1	3½ mo.	Mild hypertrophic and superficial gastritis	Active	—
Patients with Duodenal Ulcer, no Control Gastroscopy, Vagotomy, Alone or with Gastroenterostomy										
10 C. F. K.	M 35	0	.....	.....	Thoracic	9	5 mo. 7 mo. 8 mo. 12 mo. 14 mo. 16 mo. 18 mo. 18½ mo. 26 mo.	Moderate, superficial gastritis Moderate, superficial gastritis, lesser curvature Normal Mild, superficial gastritis Mild, superficial gastritis Normal Normal Moderate, superficial gastritis Mild, localized, superficial gastritis	Slight Moderate Peristalsis was active at the third examination and remained active	+ — — — — — — — —
11 N. W.	M 51	0	.....	.....	Thoracic; later gastroenterostomy	1	2½ yr.	Normal	Active	—
12 R. K.	F 44	0	.....	.....	Abdominal and gastroenterostomy	1	12 mo. 5½ mo.	Moderate, superficial gastritis; hyperemic mucosa Essentially normal; gastric ulcer in lesser curvature, midportion of stomach	Active Active	— —
13 W. R.	M 32	0	.....	.....	Abdominal					
14 M. D.	M 35	0	.....	.....	Thoracic; later gastroenterostomy	3	2 yr., 8 mo. 2 yr., 10 mo. 3 yr.	Moderate, superficial gastritis Moderate, superficial gastritis, upper two thirds of stomach Moderate, superficial gastritis, upper two thirds of stomach	Active throughout	— —
		1,650 r to upper two thirds of stomach 1 yr. before operation								
Patients with Duodenal and Gastric Ulcers										
15 T. D.	M 40	1	2 days	Benign ulcer, lesser curvature, above angulus; mucosa normal	Abdominal and gastroenterostomy	1	14 days	Normal; gastric ulcer almost healed	Active	—
16 R. P.	M 39	2	7 days 5 days	Mixed gastritis, mild; 2 small ulcers in midportion, body of stomach	Abdominal and gastroenterostomy	1	4 wk.	Mild hypertrophic and superficial gastritis; ulcers healed	Absent	Slight
17 J. C.	M 31	0	.....	.....	Abdominal	1	2 mo.	Small (8 × 4 mm.) ulcer at angulus; normal mucosa (ulcer smaller at roentgenoscopic examination than at original examination)	Active	—
		Roentgen irradiation 1,656 r to upper two thirds of stomach 3 wk. before operation								

CASE 13.—W. R., a 32 year old man, underwent a transabdominal vagotomy, after having experienced ulcer distress for eight years. Symptoms recurred several months after operation, increased in intensity and, five months after operation, culminated in the passage of several tarry stools. The result of the insulin test was negative; the output of acid in the nocturnal gastric secretion was reduced. Gastroscopy demonstrated a benign ulcer, approximately 2 to 3 cm. in diameter, on the anterior wall of the lesser curvature, in the midportion of the stomach. The mucosa appeared essentially normal; peristalsis was noted in the antrum. A partial gastric resection was performed, with the removal of a benign ulcer. The microscopic appearance of the stomach is described later in this report.

Gastric Ulcer.—The observations in the 9 cases of benign gastric ulcer are presented in individual case reports and are also summarized briefly in table 2.

CASE 18.—In G. C., a man of 67, gastroscopy one week before transabdominal vagotomy had demonstrated a benign ulcer on the anterior wall of the lesser curvature of the stomach and moderate superficial and atrophic gastritis. Partial healing of the ulcer was noted one month after operation; the mucosa appeared normal, despite gastric retention. The ulcer was not visible five months after operation. The mucosa in some areas appeared normal, while in other regions it was covered with mucus. Gastric retention persisted, although peristaltic activity was observed in the antrum.

CASE 19.—A. P., a man of 45, had received a total of 1,635 r (depth dose) in divided amounts to the fundus and body of the stomach three years before operation for the purpose of reducing gastric secretion. Six gastroscopies during this period disclosed a benign ulcer on the lesser curvature above the angulus, and, at different examinations, mild to moderate superficial gastritis, slight atrophy and (on one occasion) a normal mucosa. The ulcer, present three weeks before transthoracic vagotomy, had healed completely one month after operation. The mucosa appeared irregularly reddened. Peristalsis was absent, and gastric retention was pronounced.

CASE 20.—H. A., a man of 43, received a total of 1,160 r (depth dose), applied in divided amounts to the stomach approximately four years before transthoracic vagotomy; a second course of irradiation, comprising 1,600 r, was administered one month after operation. Fourteen gastroscopies performed during the preoperative period demonstrated the healing and recurrence of a benign ulcer on the lesser curvature of the stomach, at the angulus. The mucosa initially appeared normal. Approximately two and one-half years before vagotomy, an hourglass deformity had developed in the midportion of the stomach; subsequently, atrophy was observed in the lower segment and superficial inflammation in the upper pouch. Severe hypertrophic and superficial changes were noted approximately one year before operation. Three gastroscopies were performed after vagotomy. Peristalsis was diminished or absent; gastric retention was pronounced. The hourglass deformity persisted; only the upper segment was visualized. Four months after vagotomy the mucosa in some areas appeared entirely normal. In other areas it was dull, reddened and hemorrhagic; there was a questionable superficial erosion on the lesser curvature near the cardia. At seven months the mucosa presented a dull, thickened appearance. At nine months dulness and hyperemia were noted in some regions and a normal mucosa

TABLE 2.—*Gastroscopic Appearance of Gastric Mucosa Before and After Vagotomy in 9 Patients with Benign Gastric Ulcer*

		Before Vagotomy				After Vagotomy				Gastroscopic Observations	
Case	Sex and Age	No. of Examinations	Interval Before Operation	Gastric Mucosa	Type of Vagotomy	No. of Examinations	Postoperative Interval	Gastric Mucosa	Ulcer	Peristalsis	Gastric Retention
18 G. C.	M 67	1	7 days	Ulcer; moderate, superficial and atrophic gastritis	Abdominal	2	1 mo. 5 mo.	Normal Moderate, superficial gastritis	Smaller Healed	Shallow Active	+ +
19 A. P.	M 45	6	2¼ yr.	Ulcer; mild to moderate, superficial gastritis; atrophic changes; normal mucosa (once)	Abdominal	1	1 mo.	Mild, superficial gastritis	Healed	Absent	+
20 H. A.	M 43	14	4½ yr. to 2 wk.	Ulcer; initially, normal mucosa; later, hourglass contraction; superficial and atrophic changes; severe superficial and hypertrophic gastritis	Abdominal	3	4 mo. 7 mo. 9 mo.	Hourglass contraction; normal areas; mucosa in areas dull, reddened and bled easily Moderate, superficial gastritis Irregular, superficial gastritis, areas of normal mucosa	Superficial Healed Healed	Shallow Shallow Shallow	+ + +
21 G. K.	M 39	6	3¾ yr. to 2¼ yr.	Ulcer; severe, superficial gastritis; severe, hemorrhagic, erosive hypertrophic gastritis	Abdominal	5	2 mo. 6 mo. 18 mo. 2½ yr. 3 yr., 2 mo.	Moderate, superficial and hypertrophic gastritis Moderate, superficial gastritis Mixed gastritis Same Hourglass contraction; mixed gastritis	Healed Healed Healed ? Recurrence	Shallow Shallow Shallow Active Active	+ + + + +
22 J. A.	M 46	13	2 yr. 3 mo. to 2 wk.	Ulcer; varying degrees of hypertrophic gastritis, often severe; hemorrhages; erosions	Thoracic	9	3½ mo. 5½ mo. 8½ mo. 11 mo. 13 mo. 16 mo. 22 mo. 23 mo. 4 yr., 8 mo.	Mild hypertrophic gastritis Moderate, superficial gastritis Hemorrhages; superficial gastritis Moderate, superficial gastritis Severe, superficial gastritis Mild, superficial gastritis Superficial, erosive gastritis Severe, superficial gastritis; 1 erosion Erosion above angulus; superficial and atrophic gastritis	Healed Healed Shallow, at angulus Healed Healed Healed Healed Healed Healed	Not known before last examination Active	 ..
23 J. W.	M 70	10	25 mo. to 2 wk.	Ulcer; mild, superficial gastritis; hemorrhages, moderate hypertrophic gastritis 2 wk. before operation	Thoracic	2	2 wk. 2 yr., 10 mo.	Mild, superficial gastritis Large amount of mucus; mucosa essentially normal	Healed Healed	.... Active	Slight Slight
Gastroenterostomy 8 yr. before vagotomy											
24 A. F.	M 37	6	6½ yr. to 1 wk.	Mild to moderate hypertrophic gastritis; hemorrhages; later, mild atrophy	Abdominal and gastroenterostomy	1	21 mo.	Normal	Healed	Active	..
Intrapylorie ulcer with gastric retention											
25 A. N.	F 66	0	.....	.....	Abdominal, local excision of ulcer	1	3 mo.	Hourglass deformity; mucosa of upper segment normal	Healed	....	+
26 E. T.	F 45	0	.....	.....	Abdominal	1	18 mo.	Moderate atrophy, midportion; rugae normal	Recurrence	Active	—

in other areas of the upper pouch. There was no evidence of ulcer. The acid response to histamine was approximately the same as before vagotomy.

CASE 21.—G. K., a man of 39, with diabetes mellitus; gastroscopy (on six occasions) before transthoracic vagotomy had demonstrated a very large, presumably benign ulcer on the posterior wall of the midportion of the stomach; severe gastritis was present, characterized by diffuse hyperemia, swollen—almost polypoid—folds and excessive amounts of mucus; pronounced hypertrophic, hemorrhagic, erosive gastritis was observed on one occasion. An interval of two and one-fourth years elapsed between the final control gastroscopy and vagotomy. Five examinations, performed during a postoperative period extending from two months to more than three years, demonstrated mixed hypertrophic and superficial gastritis, shallow peristalsis and retention of food and mucoid material. These changes persisted until three years and two months after vagotomy. Gastroscopy now disclosed a contraction of the midportion of the stomach, taking the form of a large fold extending from the anterior to the posterior wall. The fold was surmounted by a large, dark gray ulcer, approximately 1.5 cm. in diameter, whose border was slightly irregular in contour, but sharply demarcated. The mucosa in some areas appeared normal; in others, dull and reddened, and elsewhere edematous with adherent mucus. The maximum free acidity after histamine stimulation was similar to that noted before operation.

CASE 22.—J. A., a man of 46, had had a total of 1,325 r (depth dose) applied in divided amounts to the fundus and body of the stomach approximately two years before operation. The maximum free acid (histamine test) three months later had decreased from 110 to 20 clinical units, but the quantity soon returned to its original level. Thirteen gastroscopies demonstrated the healing and recurrence of a benign ulcer on the lesser curvature, above the angulus. Severe hemorrhagic, hypertrophic gastritis was noted on seven occasions, and erosions were seen twice. Nine gastroscopies, performed during a period of three and one-half months to four and three-fourths years after transthoracic vagotomy, disclosed a variable, but occasionally severe, superficial gastritis. Approximately eight months after operation a shallow ulceration was noted at the angulus. Gastroscopy four years and eight months after operation demonstrated vigorous peristalsis, a grayish mucosa with hemorrhages and adherent mucus, and a small erosion in the area of the ulcer, above the angulus. Free hydrochloric acid was present in the gastric contents after histamine stimulation.

CASE 23.—J. W., a 70 year old man, with a recurrent ulcer of twenty-five years' duration, had undergone two operations elsewhere (local excision of the ulcer and, later, gastroenterostomy). Two courses of roentgen irradiation were applied to the fundus and body of the stomach. The first, of 1,500 r (depth dose), produced transient anacidity, with temporary healing of the ulcer; the second, given eighteen months later with a total dose of 1,671 r, had no demonstrable effect on gastric acidity. Ten gastroscopies revealed, during a period of two years, the healing and recurrence of a large gastric ulcer above the gastroenterostomy stoma, superficial gastritis and mucosal hemorrhages; a moderately severe, hemorrhagic, hypertrophic gastritis was present two weeks before transthoracic vagotomy. Two gastroscopies were performed subsequently. The examination two weeks after operation demonstrated healing of the ulcer, mild superficial gastritis and slight gastric retention. Two years and ten months later the mucosa appeared normal, despite persistent gastric retention; the ulcer had not recurred.

CASE 24.—A. F., a man aged 37, had been treated for an intrapyloric ulcer, with gastric retention, for eight years. A total of 1,350 r (depth dose) had been directed to the fundus and body of the stomach for the purpose of reducing

gastric acidity. Six gastroscopies, prior to transabdominal vagotomy and gastroenterostomy, initially revealed mild to moderate hemorrhagic, hypertrophic, gastritis; slight atrophy developed during the irradiation. Twenty-one months after operation the gastric mucosa appeared normal.

CASE 25.—A. N., a housewife aged 67, had undergone a transabdominal vagotomy and, two months later, the local excision of a benign gastric ulcer. A pronounced hourglass deformity of the stomach, with gastric retention, developed subsequently. Gastroscopy three months after vagotomy revealed a normal mucosa in the upper portion of the stomach; the lower segment was not visualized, because of the greatly narrowed lumen.

CASE 26.—E. T., a housewife aged 45, had experienced ulcer distress since 1922. A gastroenterostomy had been performed in 1932. The normal continuity of the bowel was reestablished in January 1945. Roentgen irradiation had been directed to the stomach, but the amount given and the effect on gastric secretion could not be ascertained; the patient first appeared at the University Clinics two and one-half years later. Roentgenoscopy demonstrated a gastric ulcer, and a transabdominal vagotomy was performed. After operation, the result of the insulin test was negative, and the nocturnal gastric secretion was greatly reduced. The gastric ulcer was not demonstrable roentgenologically three months later. The patient remained well for eighteen months; ulcer distress then reappeared. The insulin test again yielded a negative response. Free acid was present in the gastric contents after histamine stimulation. Gastroscopy demonstrated a superficial ulcer on the lesser curvature, above the angulus. The gastric rugae appeared normal; moderate atrophy had occurred in the midportion of the stomach. Active peristalsis was observed in the antrum. Gastric resection was performed eight days later, the distal third of the stomach being removed; the microscopic features are described later in this paper.

Comment: Gastric retention was observed in 6 of the 8 patients of this group treated by vagotomy alone. The early observations in case 22 were incomplete in this regard; however, retention was not present four years and eight months after operation. Gastric retention was not present in 1 patient undergoing both vagotomy and gastroenterostomy or, eighteen months after operation, in another patient treated by vagotomy alone. Peristaltic activity was noted gastroscopically in 6 patients. Gastritis of varying types and severity had been observed gastroscopically in the 7 patients examined before vagotomy. Five had had irradiation directed to the upper portion of the stomach at varying intervals (usually of several years) prior to the operation. The inflammation had not changed significantly in 5 patients; the condition had apparently subsided in 1, and slight improvement was noted in another.

Control observations were not obtained in case 25, but a normal mucosa was observed after vagotomy; moderate localized atrophy was noted in case 26.

The gastric ulcers healed in all 9 patients, in 1 instance within two weeks after operation. However, a large ulcer was demonstrable in case 21, slightly more than three years after vagotomy. In case 22 the

ulcer recurred temporarily eight months after operation, and an erosion was noted four and three-quarters years after vagotomy. A superficial ulcer was noted gastroscopically in case 26, eighteen months after vagotomy. The insulin test was performed after operation on eight patients, with negative results in 7 and a positive response in 1 (case 25).

Miscellaneous.—CASE 27.—M. S., a woman aged 45, with vague abdominal symptoms, was subjected to a transabdominal vagotomy in an unsuccessful effort to relieve the discomfort. Gastroscopy fourteen months later demonstrated a normal mucosa and active peristalsis. The result of the postoperative insulin test was negative.

General Comment.—The present observations indicate that vagotomy does not alter significantly the gastroscopic appearance of the stomach. The mucosa seemed relatively unchanged in 13 of the 18 patients examined before and after operation; the original diagnoses had been normal mucosa in 5 cases, superficial gastritis in 3, hypertrophic inflammation in 2 and mixed gastritis in 3. An essentially normal mucosa was observed after vagotomy in 5 cases, of which the preoperative impressions had included hypertrophic gastritis, in 3, and superficial and mixed gastritis, in 1 each. The significance of this apparent improvement seems questionable, however, in view of the unpredictable variations in the type and severity of gastritis encountered spontaneously.[6] An additional factor may be the individual differences in gastroscopic interpretation, recently emphasized by McGlone;[7] although the majority of the postvagotomy examinations were made by one of us (J. B. K.), five physicians had participated in the preoperative studies.

In the present series, the prolonged retention of food and mucoid material apparently did not predispose to gastritis, nor did it seem to intensify a preexistent inflammation, as determined gastroscopically. The results of this study are in general agreement with the observations of Paulson and Gladsden.[4] Asher[5] concluded, however, that vagotomy produced definite gastritic changes; these occurred with less frequency when a gastroenterostomy was established in addition to the section of the vagus nerve. The rather high incidence of hypertrophic gastritis and superficial erosions in Asher's study is of interest. In contrast, the incidence and severity of gastritis in the present investigation did not differ significantly in relation to the presence or absence of gastroenterostomy; hypertrophic changes were not commonly encountered. However, recurrent ulcers were noted after vagotomy in 4 patients (cases 4, 13, 21 and 26). In case 22 erosions were observed in the orig-

6. Maimon, S. N., and Palmer, W. L.: Chronic Gastritis: Observations on Its Course and Significance, Gastroenterology **6**:511, 1946.

7. McGlone, F. B.: Observations on Gastritis Based upon Experience in a General Hospital in the South Pacific, Gastroenterology **10**:681, 1948.

inal area of the ulcer at intervals of twenty-two months, twenty-three months and four years eight months after vagotomy; erosions had also been noted before operation. In several patients the gastric mucosa appeared hemorrhagic at times, both before and after vagotomy. The histologic appearance of the stomach after vagotomy, as will be described later in this paper, usually did not differ strikingly from that observed in patients with ulcer having intact vagus nerves and in persons with no history of gastrointestinal disease.

With regard to prolonged gastroscopic observation, 5 patients (cases 4, 21, 22, 23 and 24) reexamined from twenty-one months to four years and eight months after vagotomy manifested active peristalsis, although a varying degree of retention was present in 3. Gastritis persisted in 3 and apparently subsided in 2 of 4 patients on whom gastroscopy was performed only after vagotomy, at postoperative intervals of eighteen months or more, a normal mucosa, localized atrophy and superficial gastritis were observed in 1 each, and both a normal mucosa and mild superficial changes in 1.

HISTOLOGIC APPEARANCE OF STOMACH AFTER VAGOTOMY

The stomach was examined histologically after vagotomy in 11 patients. The observations are presented in individual case reports.

CASE A.—O. K., a 59 year old housewife with diabetes and hypertension, experienced pain from an ulcer for three weeks. Roentgenoscopic examination disclosed a duodenal ulcer, and symptoms were relieved by medical treatment. The patient first appeared at the University Clinics one year later, because of recurrent distress. A transabdominal vagotomy and posterior gastrojejunostomy were performed after one month. However, the patient died of atelectasis and pneumonia one week after the operation, despite bronchoscopic aspiration and the administration of penicillin. At autopsy, the vagotomy anatomically appeared complete. A large, healing ulcer was present in the duodenal bulb. Additional diagnoses included severe arteriolosclerosis and arteriosclerosis of the pancreatic vessels, severe fibrosis and atrophy of the pancreas, bilateral bronchopneumonia of the lower lobes, acute purulent bronchitis, severe generalized arteriolosclerosis, moderate arteriosclerosis and hypertrophy of the left ventricle. The gastric mucosa presented no gross abnormality. Histologic examination demonstrated an essentially normal mucosa, with minimal cellular infiltration. The gastric glands and crypts were well preserved. The parietal and chief cells were abundant and appeared normal.

CASE B.—M. C., a 54 year old woman, had experienced ulcer distress for ten years. Roentgenoscopic examination demonstrated a benign gastric ulcer; the ulcer was excised and a vagotomy performed. A biopsy of antral mucosa adjacent to the ulcer disclosed moderate chronic gastritis. A posterior gastroenterostomy was established several weeks later because of obstruction. The patient died of a reaction to the infusion of plasma one month after vagotomy. Autopsy disclosed hemoglobin precipitate in the renal tubules. The vagotomy appeared anatomically complete. The pylorus was almost completely obstructed by a mem-

brane composed of gastric mucosa on the superior surface and duodenal mucosa on the inferior surface, the channel through this valvular shelf measuring 2 mm. in diameter; this deformity seemed attributable to the local excision of the ulcer. Grossly, the gastric mucosa appeared smooth, but otherwise normal. Microscopic examination of the mucosa of the fundic and prepyloric regions disclosed a minimal gastritis, a few cystic glands, hypertrophy of occasional muscle fibers and congestion of the submucosal veins. The parietal and chief cells were normal. Acid-secreting cells were present also in glands on the duodenal border of the pylorus.

CASE C.—F. K., a 59 year old woman, on roentgenoscopic examination presented a small ulcer on the lesser curvature of the stomach and narrowing of the antrum. Gastroscopy disclosed mild superficial gastritis. A transabdominal vagotomy and posterior gastroenterostomy were performed two weeks later. Microscopic examination of a specimen from the fundus of the stomach indicated minimal chronic gastritis, the cellular infiltrate consisting chiefly of plasma cells and eosinophils (fig. 1*A*). The parietal and chief cells were normal in appearance and distribution (fig. 1*B*). The patient died five months later of a gliobastoma multiforme of the left temporal lobe. Autopsy revealed, in addition, lipid bronchopneumonia and an acute gangrenous abscess in the lower lobe of the right lung. Anatomically the vagotomy appeared complete. Grossly, the gastric mucosa, except for the scar of a healed prepyloric ulcer, was normal. Striking changes were observed microscopically, in comparison with the appearance of the control biopsy specimen obtained five months earlier. The stomach now was involved diffusely by an unusually severe, chronic gastritis, most pronounced in the antrum (fig. 2); there was much interstitial infiltration of the entire gastric wall, chiefly by round cells. Cystic changes were prominent, but so-called intestinalization was not present; the thickness of the mucosa was approximately normal. Of particular interest were the pronounced hyperchromatism of glands and the significant decrease in number of acid-secreting cells; these cells in many areas were poorly differentiated and difficult to identify (fig. 3).

CASE D.—G. S.,[8] a 46 year old man, underwent a partial gastrectomy after twenty years of recurrent distress from a duodenal ulcer; a jejunal ulcer developed several weeks later. The ulcer healed after transthoracic vagotomy but recurred six months later, complicated by a gastrojejunocolic fistula. The fistula was repaired, and several previously uncut vagus fibers were excised. However, the secretion of hydrochloric acid remained excessive. The patient died of a massive hemorrhage, five days after the second operation and six and one-half months after the initial vagotomy. Autopsy revealed an ulcer crater, 8 by 5 cm., at the margin of the gastroenterostomy site, with an eroded artery in its base. No intact vagus fibers were grossly visible, but apparently viable nerves were identified histologically between the muscle layers of the esophagus and the stomach. The pancreas contained an islet cell carcinoma; one metastatic lesion was present in the liver. Grossly, the gastric mucosa appeared normal. Histologic examination disclosed rather severe superficial gastritis and occasional cystic glands. The parietal and chief cells were abundant and well preserved. This case was described in more detail in another paper.[8]

CASE E.—R. B., a 66 year old man, had experienced symptoms referable to the gastrointestinal tract for thirty years and known ulcer distress for twenty years.

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8. Kirsner, J. B.; Levin, E., and Palmer, W. L.: Observations on the Excessive Nocturnal Gastric Secretion in Patients with Peptic Ulcer, Gastroenterology **11**:598, 1948.

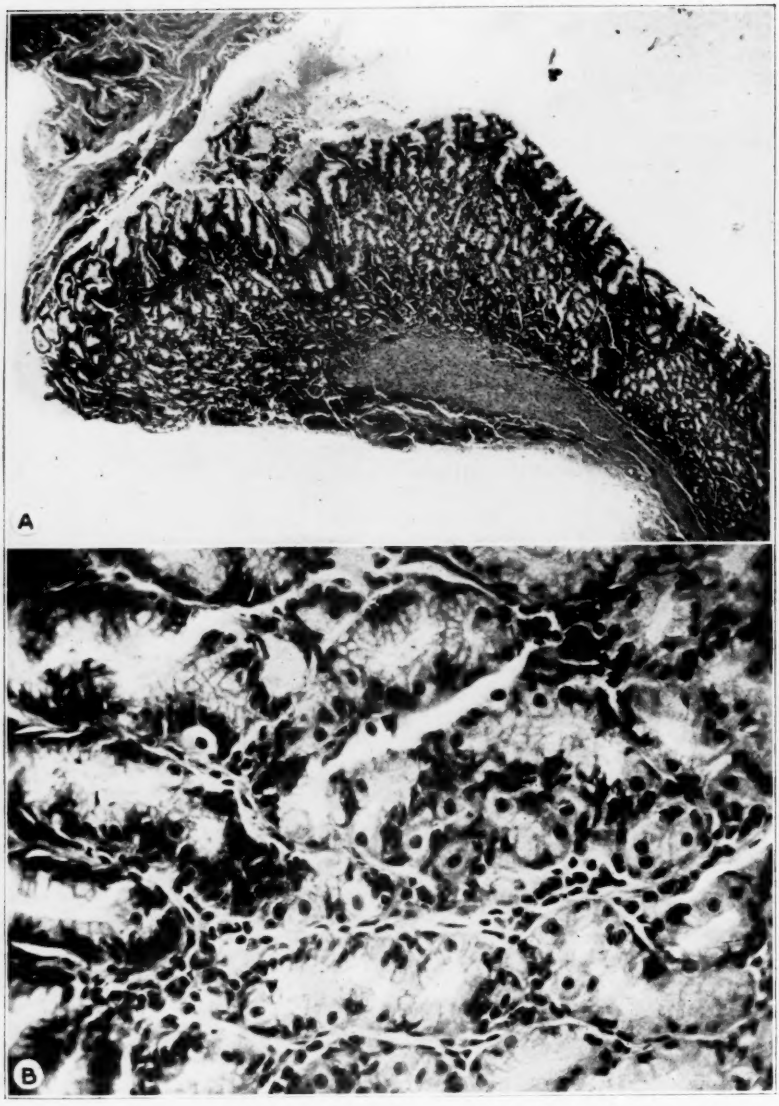

Fig. 1 (case C).—Biopsy specimen of mucosa of the fundus of the stomach, taken at the time of vagotomy. *A*, minimal gastritis; preservation of the normal glandular pattern (×62). *B*, numerous normal-appearing parietal cells in an essentially normal gastric mucosa (×310).

Fig. 2 (case C).—Gastric mucosa at autopsy, five months after vagotomy. Above, fundic mucosa; severe, chronic gastritis with cystic glands; the loss of the mucus-secreting layer is a postmortem artefact. Below, antral mucosa; severe, chronic, cystic gastritis. × 50.

A transabdominal vagotomy was performed at another hospital, but symptoms recurred within two weeks. Roentgenoscopic examination disclosed an ulcer crater in an undeformed duodenal bulb, and a second vagotomy, together with an anterior gastroenterostomy, was accomplished. Complete obstruction of the gastroenterostomy opening occurred after operation, necessitating side to side anastomoses in the jejunum and ileum. The patient died several days later, after a reaction to the administration of pooled plasma; death occurred one year after the initial operation and fifteen days after the second vagotomy.

Autopsy indicated that the vagotomy was complete anatomically. The only evidence of the former duodenal ulcer consisted of a focus of epithelium, 1 cm. in diameter, thinner than the surrounding mucosa, from which folds radiated.

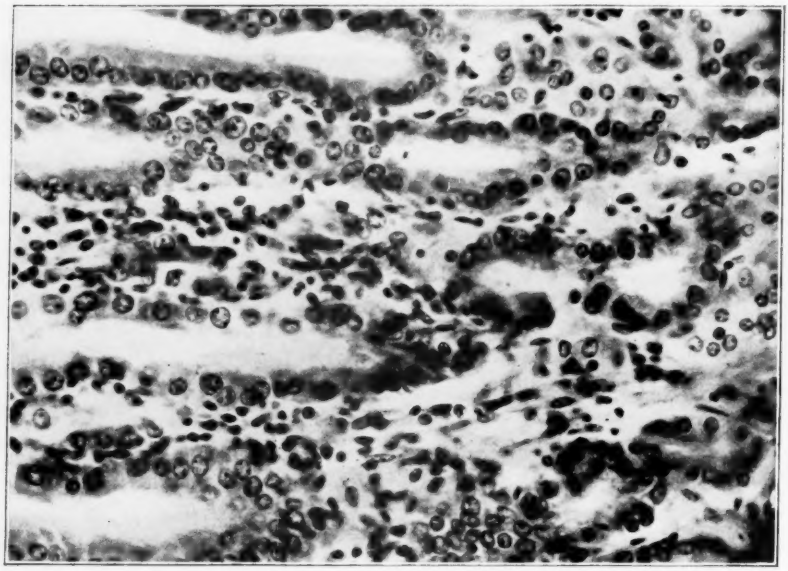

Fig. 3 (case C).—Fundic mucosa at autopsy. Most of the parietal cells have disappeared; the glands are lined with a simplified type of epithelium. × 350.

Additional diagnoses included massive aspiration pneumonia of the upper and middle lobes of the right lung, pulmonary edema and thrombosis of the mesenteric veins. The gastric mucosa contained minute erosions and hemorrhages and appeared edematous in the region of the gastroenterostomy wound. Histologically, the mucosa appeared essentially normal, with only minimal interstitial infiltration with round cells. One small area of mild atrophy was noted on the lesser curvature. Parietal and chief cells were abundant and appeared normal.

Case F.—E. M.,* a 63 year old man, had required closure of a perforated duodenal ulcer one year after the onset of symptoms. Ulcer distress recurred, and a transabdominal vagotomy and posterior gastroenterostomy were performed one

year later. A jejunal ulcer developed within six months; the result of the insulin test was positive. A second vagotomy was then accomplished, with the excision of a large fiber in the posterior wall of the esophagus and of smaller branches below the esophagus. Roentgen radiation, a total of 1,656 r (depth dose), was applied to the fundus and body of the stomach for the purpose of reducing gastric acidity. The result of the insulin test remained positive and the output of hydrochloric acid excessive. Ulcer distress recurred several months later, and a fourth operation was performed, at which time a large jejunal ulcer perforated spontaneously. The jejunum containing the anastomosis and the perforation was resected, and an end to end jejunostomy was established. The patient was readmitted to the hospital three months later, because of several mild hematemeses, and died soon thereafter, of a "toxic reaction," one year and three months after the initial vagotomy and six months after the second vagotomy.

Autopsy demonstrated intact vagus fibers passing along the esophagus into the stomach. The duodenal ulcer was healed. Additional findings included mild toxic encephalopathy of the cerebral cortex, bronchopneumonia with early abscess formation, a benign hepatoma and an old occlusion of the right coronary artery. The gastric mucosa contained multiple petechial hemorrhages. Histologic examination disclosed only minimal cellular infiltration; no evidence of atrophy was noted. The parietal and chief cells were numerous and well preserved.

Case G.—S. K., a 39 year old man, had experienced ulcer distress for twelve years; a duodenal ulcer was demonstrated roentgenologically. The symptoms were relieved completely, and the patient gained approximately 30 pounds (13.6 Kg.) in weight after a transabdominal vagotomy. No free acid was present in the nocturnal gastric secretion. Results of insulin tests, made after operation and eighteen months later, were negative. The patient died of bullet wounds approximately eighteen months after operation.

At autopsy, no intact vagus fibers were grossly visible. Small, nonmyelinated, apparently normal nerve trunks were observed histologically in the periesophageal tissues; several of these fibers were buried deeply in the muscle layers of the esophagus. Grossly, the stomach appeared normal except for slight localized thinning of the mucosa near the pyloric ring. The gastric wall was involved diffusely by a rather severe gastritis, with pronounced cellular infiltration, predominantly of lymphoid cells; this was most pronounced in the superficial zone, but in many areas the infiltrate reached and penetrated the muscularis mucosae. Large and small lymphoid follicles were situated along the muscularis mucosae. Cystic glands and focal atrophy of the mucosa were observed near the cardiac orifice. The mucosa elsewhere was not atrophic. The mucosa of the fundus was thick and contained many normal-appearing parietal and chief cells. The condition of the gastric pits could not be evaluated because of the postmortem loss of epithelium. Toward the antrum, the exudate was more pronounced; an occasional cystic gland was noted. Considerable adipose tissue was present in the submucosa of the pyloric ring and in the submucosa of the entire small intestine. The first portion of the duodenum contained several areas of scarring, with regeneration of the surface epithelium and of Brunner's glands.

Case H.—N. K., a 51 year old man, had experienced ulcer distress for eight years. Roentgenoscopic examination demonstrated an ulcer crater in a deformed duodenal bulb. Roentgen radiation, a total dose of 1,671 r, was applied to the fundus and body of the stomach. The ulcer recurred eight months later, and a transthoracic vagotomy was performed. Gastroscopy, performed one week before operation, had demonstrated an extensive hypertrophic gastritis involving the body

and antrum of the stomach. The result of the postoperative insulin test was negative. The ulcer healed and did not recur. The patient died two years and three months later, of extensive metastases from a chondrosarcoma of the left tibia. Autopsy demonstrated lesions in the left hip, regional and retroperitoneal lymph nodes, kidneys, liver, diaphragm, heart, thyroid, lungs, ribs and cranium. There were no intact vagus fibers grossly; histologic examination, however, indicated the presence of nerve fibers. The upper two thirds of the stomach appeared normal in size, shape and tone; the distal third, however, was contracted to approximately the caliber of the first portion of the duodenum. The pylorus was normal. The duodenal ulcer was healed. Multiple hemorrhages had occured in the gastric mucosa; the rugae appeared somewhat flattened. Histologic examination disclosed minimal superficial gastritis in the fundus, slight thinning of the mucosa of the lesser curvature and early atrophy and slight round cell infiltration of the mucosa adjoining the pylorus. The parietal and chief cells were abundant and well preserved.

CASE 13.—Clinical details in this case have been recorded previously. A partial gastric resection was performed five and one-half months after vagotomy for a duodenal ulcer. The distal half of the stomach was removed; a benign ulcer was present on the lesser curvature, 7.5 cm. above the pylorus. Because of adhesions it was not possible to determine the presence or absence of intact vagus fibers anatomically; however, the insulin test had yielded a negative acid response. The stomach was involved irregularly by moderately severe gastritis, with infiltration of plasma cells and eosinophils and scattered lymphoid follicles. Accumulations of leukocytes, including polymorphonuclear cells, were present in numerous crypts. The mucous cells on the surface were well preserved. Focal thinning of the mucosa had occurred in the uppermost portions of the resected specimen, and the glands in these areas were shortened. Most regions, however, contained numerous, normal-appearing parietal and chief cells. The mucosa near the entrances of the gastric pits was normal; at deeper levels the glands appeared hyperchromatic, and the cells were crowded, the cellular density being interpreted as compatible with very early atrophy of the gastric mucosa.

CASE 26.—Clinical features in this case have been summarized earlier in this paper. A gastric resection was performed eighteen months after transabdominal vagotomy; the distal third of the stomach, containing a small erosion on the posterior wall, was removed. The gastric rugae grossly appeared normal. Histologic examination revealed a relatively normal mucosa. The gastric glands and crypts were well preserved; slight fibroplasia was evident at the bases of the glands. There was a minimal amount of cellular infiltrate, slightly more being present in the antrum. The mucous cells were well preserved. The parietal and chief cells were abundant and appeared normal. Glands bearing both acid and peptic cells, intermixed with seromucinous glands, were observed to extend to the pyloric ring.

CASE 4.—Clinical features of this case have been described. A large, benign ulcer developed four years and three months after transthoracic vagotomy for a duodenal ulcer. The result of the insulin test was positive. A partial gastric resection was performed, and an intact vagus fiber was severed. Histologic examination disclosed diffuse chronic gastritis, most pronounced in the region of the ulcer and characterized by increased cellularity of the stroma and by small numbers of leukocytes in the lumens of the glands. The cellular infiltrate in many areas extended into the muscularis mucosae. There were many basally located mucosal lymphoid nodules, especially near the ulcer. Minimal atrophy was present. The parietal, chief and mucous cells were abundant and well preserved.

Comment.—The histologic appearance of the stomach after vagotomy in 9 of the 11 patients did not differ from that often observed in patients with peptic ulcer and with intact vagus nerves, and, indeed, in persons with no history of gastric disease. The vagotomy appeared complete anatomically in 4 of the 8 bodies examined at autopsy and incomplete in 4. No unusual atrophy of the mucosa had taken place. The parietal and chief cells were normal in appearance and distribution. Evaluation of the mucus-secreting cells was possible only in the 3 patients undergoing gastric resection; in these they appeared normal.

Extensive round cell infiltration, conspicuous cystic formation and degeneration and diminution in the number of acid-secreting cells were observed in 1 patient (case C) five months after complete vagotomy. The relation of these changes to the vagotomy is difficult to evaluate conclusively in view of the concomitant presence of a brain tumor and the various complicating infections. However, in our experience, the degeneration and disappearance of parietal cells are rare in a mucosa of normal thickness. The gastritis in cases G and 13 and the erosions in case E seemed more pronounced than is usual; however, similar changes have been observed occasionally in patients with ulcer and intact vagus nerves and in persons with no history of gastric disease. The increased amount of fat in the submucosa of the pylorus and the entire small intestine in S. K. is of interest; the significance of this observation and its relation to the vagotomy are not clear at present. In general, the histologic evidence, in support of the gastroscopic results, suggests that vagotomy usually does not produce striking changes, either grossly or microscopically detectable, in the appearance of the stomach.

Two additional observations are of interest. In case H, two years and three months after vagotomy, the distal third of the stomach was contracted to the diameter of the duodenum, and the cardiac and pyloric orifices were normal. Multiple hemorrhages were present in the gastric mucosa of 2 patients, and hemorrhages and minute erosions in 1 patient; these probably represent antemortem changes, not attributable to the vagotomy.

CONCLUSIONS

1. Vagotomy usually does not alter significantly the gastroscopic appearance of the gastric mucosa.

2. Peristalsis frequently is observed in the antrum after vagotomy. However, gastric retention persists for a time in most patients without gastroenterostomy.

3. The prolonged retention of food and mucoid material apparently does not cause gastritis or accentuate preexistent gastritis.

4. Benign gastric ulcer may develop or recur from several months to several years after vagotomy.

5. The histologic appearance of the stomach at intervals of one week to four years and eight months after vagotomy usually does not differ significantly from that often observed in patients with ulcer and intact vagus nerves, and in persons with no history of gastric disease. No unusual atrophy occurs, and the parietal and chief cells are normal in appearance and distribution.

6. Rarely, severe gastritis and degeneration of the acid-secreting cells may be observed after vagotomy; in the 1 such case in this series, the relation of the changes to the operation could not be evaluated conclusively because of the presence of concomitant disease.

HYSTERICAL TYPE OF NONGASEOUS ABDOMINAL BLOATING

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IN 1911, I saw a psychopathic woman, past the menopause, who, with her protuberant abdomen, was sure that she was pregnant by the Holy Spirit. She insisted on going to a lying-in hospital and was outraged when told that she was not going to have a baby. I learned then that a bloated abdomen can be produced purely by nervous means. Later I saw an occasional nervous, unhappy woman who during the day would become more and more bloated, until by evening she would appear about eight months pregnant. The abdomen usually became flat during the night. Soon I began to realize that in these cases the cause could not be gas. Why? Because (1) a roentgenogram of the enlarged abdomen showed that there was no excess of gas in the stomach or bowel, and (2) as the swelling went down, sometimes suddenly, there was no passage of flatus.

That there was no causative organic disease in the abdomen was indicated by the fact that in almost every case several exploratory operations had failed to reveal anything significant. Usually the appendix, uterus and gallbladder had been removed, without avail. One woman with a particularly stormy form of this syndrome, whom I saw with Dr. Bargen, had had her abdomen opened so many times that she had finally lost count.

I now report 92 cases of this neurotic or hysterical type of nonflatulent bloating. The syndrome is similar to that described in the past under the terms "phantom tumor," "pseudoileus" or "accordion abdomen." There are several varieties of the syndrome, some severe, painful and disabling, and others in which the distention is mild or occasional or incidental to more serious troubles. Doubtless many neurotic women occasionally bloat in this way but have so little trouble with the syndrome that they do not mention it when they go to an internist.

DEFINITION AND CLINICAL PICTURE

The essential point in all the cases described here is that the pronounced bloating is due not to any excess of gas in the digestive tract but apparently to a contraction of the muscles lining the back and the

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* A preliminary report on this subject was read at the Sixtieth Session of the Association of American Physicians, Atlantic City, N. J., May 6, 1947, and was published (Tr. A. Am. Physicians, **60**:86, 1947).

upper end of the abdominal cavity. Sometimes, in addition, there may be a relaxation of the muscles of the anterior abdominal wall. These changes, associated often with the assumption of an extremely lordotic posture by the patient, tend to throw the abdominal contents forward and somewhat downward, toward the brim of the pelvis. In one instructive case, the woman, while standing in my office, would take off a 2 inch (5 cm.) belt and instantly bloat, apparently by relaxing the anterior abdominal wall. In this instance there was no simultaneous increase in lordosis. Then the patient would put the belt on loosely; with this form of autosuggestion the muscles would contract, and the abdomen would appear normal again.

Most patients stated that at first they tended to bloat only once in months or in a year. Later the interval shortened, until the bloating sometimes came every day. This shortening of the interval is typical of those types of abdominal "storm" for which no local cause can be found.

In most cases, the swelling develops quickly after a large meal, or slowly during the afternoon, and diminishes during the night without the passage of flatus. This is a most important point diagnostically. The patient is often well between spells, with good appetite and digestion. In rare cases, there is a picture of severe constipation, with what appears to be an attack of intestinal obstruction.[1]

The Several Types of Bloating.—Before going further, it may be helpful to note that there are a number of types of bloating, and that some nongassy bloaters on occasion have one or more of the other types of abdominal swelling. Unless this fact is recognized and, while taking a history, the physician unscrambles the several stories, he may become confused.

True gassy bloating due to indigestion can be produced by (*a*) eating too much, (*b*) eating when nervously upset, (*c*) eating indigestible or poorly prepared food, (*d*) eating foods such as baked beans, onions or cabbage which are notoriously gassy, (*e*) eating too much roughage or (*f*) eating a food to which one is allergically sensitive.

There is a type of bloating that appears with some forms of diarrhea, especially sprue or slight intestinal obstruction; in cholecystitis; in constipation, or with the swallowing of large amounts of air, as when the person is chewing gum.

Three other forms of bloating associated with much gas in the bowel are due (*a*) to the physical stimulus that comes from chewing or ingesting food, (*b*) to the stimulus derived from drinking a glass of cold

1. Christianson, H. W., and Bargen, J. A.: Functional Abdominal Distention Simulating Intestinal Obstruction, Proc. Staff Meet., Mayo Clin. **6**:441-448 (July 29) 1931.

water, pop or beer and (*c*) to taking a nap. Some persons bloat so suddenly after eating or drinking that the mechanism is obviously nervous, mechanical or physical: Insufficient time elapses for a chemical effect to take place.

CLINICAL MATERIAL

I began this study by making abstracts of some 150 case records of bloaters I had seen. As I analyzed the histories, it was apparent that in some 53 cases, the clinical picture was mainly that of true flatulence, with much gas in the bowel. The patient's illness was due for the most part to such troubles as indigestion, cholecystitis, food allergy or constipation. Helpful diagnostically was the fact that many of these truly gassy bloaters could be made more comfortable with an elimination diet, a daily enema or the removal of a diseased gallbladder; the neurotic bloaters here described could be helped little if at all by such measures.

The few cases which left me puzzled were those in which a patient with what appeared, in most spells, to be the neurosis of the abdominal wall described in this report also occasionally experienced food sensitization or an overly irritable bowel, which filled with gas when the patient drank cold water, pop or beer. After the latter type of bloating there was at times passage of some flatus. I excluded reports of most of these complicated cases from this paper because I wished to keep the picture of the neurosis of the abdominal wall as clearcut as possible. Eventually I kept reports of the 92 cases which have been used in the present study.

I regret that not all cases could be studied extensively and that only certain patients could be watched through several crises of bloating. Several were seen for only one consultation on a busy day, but all had had examinations to rule out organic disease of the abdomen. From all of them, I obtained the history which is diagnosis enough, namely, that of prounounced bloating diminishing without the passage of flatus. Because not all cases were studied with equal thoroughness, I cannot express the frequency of the several symptoms in percentages; I can give only estimates of frequency, or the number of cases in which I made note of a certain symptom.

SUDDENNESS OF BLOATING AND RECESSION

Significant and interesting is the suddenness with which the abdominal wall will often expand and occasionally contract. One woman said, "I go up and down like an accordion," and, curiously, Bernheim,[2] in 1891, and Kaplan,[3] in 1900, wrote on *ventre en accordéon*. In regard to

2. Bernheim, H.: Hypnotisme, suggestion, psychothérapie, Paris, O. Doin, 1891.

3. Kaplan, L.: De la pseudotympanite nerveuse, ou ventre en accordéon, Thesis, Paris, no. 30, 1900.

another patient, a physician wrote, "The abdomen bloats suddenly and dramatically." Twelve patients said that one form of bloating came within seconds after drinking cold water (the trigger mechanism), and 15 spoke of the suddenness with which they bloated after eating or drinking. Several bloated rapidly while in my office; there was no sign to indicate that they had swallowed air. Some of these patients had to keep on hand three sets of clothes, designed for three sizes of abdomen!

Kaplan [3] told of a young man who learned the trick of bloating the upper half of his abdomen at will. He had discovered it accidentally but could not say just how it was done; he could also stop the bloating when desired. The expansion could be maintained for some time without fatigue. During this time, the boy could eat, drink even a liter of fluid, urinate or whistle.

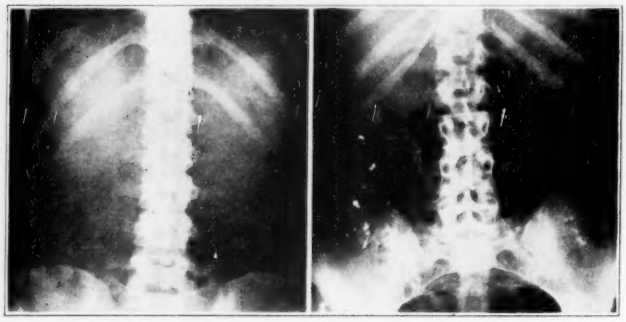

Fig. 1.—Roentgenograms made while patient was bloated. They show no excess of gas in the intestine.

ABSENCE OF GAS IN THE ABDOMEN

As already noted, an essential feature of this disease is the lack of any excess of gas in the bowel during the attacks of bloating. This was shown most convincingly by roentgenograms of the abdomen while bloating was present. Figure 1 shows how little gas was present in any part of the bowel of a typical patient.

Interestingly, one hundred years ago Sir James Y. Simpson [4] described the syndrome and knew that it was not due to gas in the bowel. To demonstrate this fact to his students, he used to place a tube in the rectum of a patient, with the outer end in a glass of water. He would

4. Simpson, J. Y.: The Obstetric Memoirs and Contributions, edited by W. O. Priestley and Horatio R. Storer, Philadelphia, J. B. Lippincott Company, 1855-1856, vol. 2, p. 101.

then give an anesthetic, and when the patient's abdomen suddenly became flat, he would call attention to the fact that no gas had come from the bowel. Janet is said to have noted this type of relief of bloating without the passage of gas. In 1881, Weir Mitchell [5] reported the case of a bloater, a woman who knew that the swelling had nothing to do with gas; in her case, it was caused by emotion. In Goldschmidt's case,[6] reported in 1922, roentgenograms showed no excess of gas in the patient's abdomen.

According to Kaplan,[3] one hundred years ago in Europe, in cases of supposed intestinal obstruction, the patient's intestines used to be punctured with a trocar. In this way it was learned that no gas was present in the cases of hysterical bloating.

MECHANISM OF BLOATING

Years ago it became clear to me, as it had to others, that in the case of the type of bloater described, the distention could not be due to gas. The next question was whether it could be due to massive angioneurotic edema of the intestine.

Edema.—Somewhat in favor of the theory of edema as a causative factor is the fact that in 16 of the cases reported in the present study, the patient tended at times to become slightly edematous, the swelling occurring all over the body or in the hands, feet or eyelids. In no case could the edema be blamed on any disease of the heart or kidneys. After a time, I saw that edema of the bowel could hardly be the explanation for the distention because of the rapidity of the rise and fall of the abdomen: Insufficient time elapsed for any change to occur in the volume of its contents.

Sudden Deflation.—On several occasions, I saw an abdomen deflate without the passage of flatus either instantly on, or a few minutes after, (1) the induction of spinal or general (ether) anesthesia or of anesthesia with thiopental sodium U. S. P. (pentothal sodium®), (2) the blocking of the splanchnic nerves with an injection of procaine hydrochloride U. S. P., (3) the onset of an attack of vomiting or (4) the reception of a hypodermic injection of morphine. In 1 case, the abdomen would promptly contract when the girl assumed the knee-chest position, and in many others, it deflated entirely, or nearly so, when the woman lay on her back, especially with the thighs flexed on the abdomen. In 1 patient under spinal anesthesia, the abdomen suddenly deflated the moment the anesthesia reached the nipples.

5. Mitchell, S. W.: Lectures on Diseases of the Nervous System, Especially in Women, Philadelphia, H. C. Lea's Son & Company, 1881, pp. 186-188.

6. Goldschmidt, W.: Ein 4 mal als Ileus laparotomierter Grenzfall von Spasmophilie und Hysterie, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **35**:544, 1922.

Because I could not imagine any way in which the volume of the abdominal contents could be so suddenly restored to normal, I concluded that no increase took place in the volume of the abdominal contents. In some cases I gained this impression also from measuring the girth of the woman's abdomen before and during bloating.

Among the writers in the past who commented on the rapidity with which the "tumor" disappeared when the patient was anesthetized, and with which it returned when she awoke were Priestley (in 1858), Wells,[7] Luton,[8] Simpson,[4] Gowers,[9] McArdle and Kolipinski,[10] Krukenberg,[11] Talma,[12] Kaplan,[3] McDonnell,[13] Da Costa,[14] Ramskill and Jones,[15] Haultain,[16] Kerr and Ferguson,[17] Purves-Stewart[18] and Garrigues.[19]

Lordosis.—Other important observations made early in the investigation were that at least 11 of these patients were more than usually lordotic when bloated, and that this factor had much to do with pushing the abdominal contents forward. Osler,[20] Gowers,[9] and Bargen and others[21] noted this "arching forward of the spine"; it was also shown, in 1884, by Krukenberg,[11] whose illustrations are reproduced here in figure 2. The woman was bloated because of her lordosis; when she straight-

7. Wells, T. S.: Diseases of the Ovaries: Their Diagnosis and Treatment, London, J. Churchill & Sons, 1865, vol. 1.

8. Luton, cited by Kaplan.[3]

9. Gowers, W. R.: A Manual of Diseases of the Nervous System, Am. ed. Philadelphia, P. Blakiston's Son & Co., 1888.

10. McArdle, T. E., and Kolipinski, L.: A Summary of the Published Cases of Phantom Tumor of the Abdomen, and the Etiology of that Condition and of Spurious Pregnancy, New York State J. Med. **43**:595, 1886.

11. Krukenberg, G.: Zur Kenntniss der hysterischen Phantomgeschwülste, Arch. f. Gynäk. **23**:139, 1884.

12. Talma, S.: Zur Kenntniss der Tympanitis, Berl. klin. Wchnschr. **23**:369, 1886.

13. McDonnell, cited by McArdle and Kolipinski.[10]

14. Da Costa, J. M.: Medical Diagnosis with Special Reference to Practical Medicine: A Guide to the Knowledge and Discrimination of Diseases, ed. 2, Philadelphia, J. B. Lippincott Company, 1866, p. 541.

15. Ramskill and Jones, cited by McArdle and Kolipinski.[10]

16. Haultain, F. W. N.: Spurious Pregnancy: A Critical Treatise from a Practical Experience, Am. J. M. Sc. **101**:342, 1891.

17. Kerr, J. M. M., and Ferguson, J. H.: Combined Text-Book of Obstetrics and Gynecology, New York, William Wood & Company, 1923.

18. Purves-Stewart, J.: The Diagnosis of Nervous Diseases, ed. 9, Baltimore, Williams & Wilkins Company, 1945, p. 661.

19. Garrigues, H. J.: A Text-Book of the Science and Art of Obstetrics, ed. 2, Philadelphia, J. B. Lippincott Company, 1907.

20. Osler, W.: The Principles and Practice of Medicine: Designed for the Use of Practitioners and Students of Medicine, ed. 3, New York, D. Appleton & Co., 1898.

21. Bargen, J. A.; Adson, A. W.; Lundy, J. S., and Dixon, C. F.: Functional Abdominal Distention Simulating Megacolon, Am. J. Digest. Dis. **3**:17, 1936.

ened her spine under anesthesia or voluntarily, the bloating disappeared. I suspect that with a little practice, any one with good muscles and a limber spine could push the anterior abdominal wall forward, just as he can pull it in until it is scaphoid (fig. 3).

That lordosis often is an important factor can be shown, as already noted, by having the bloated patient lie down (figs. 4 and 5). Especially when the knees are flexed on the abdomen, the woman will usually lose much, or all, of the bloated appearance. When she is placed on her side

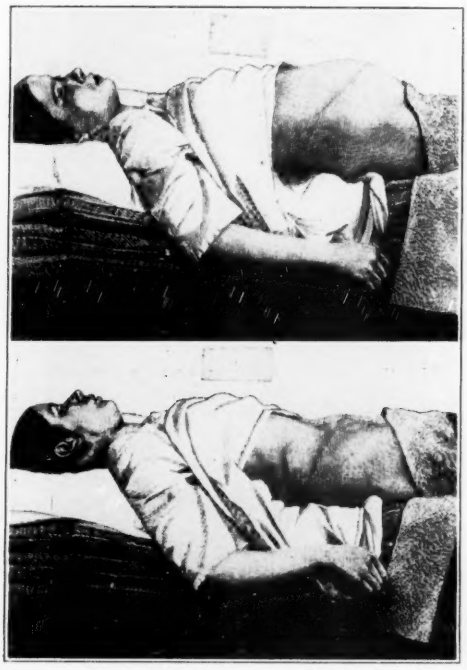

Fig. 2.—When the girl was bloated she was lordotic; when she slumped, either voluntarily or under the influence of chloroform, the bloating disappeared. (From Krukenberg.[11])

and the thighs are quickly flexed on the abdomen the lordosis is even better overcome, and a distended abdomen is likely to deflate and become soft. When the woman gets up and slumps into her old lordotic posture, the bloating usually returns (fig. 6). For years Bargen has been using this doubling up of the patient as a diagnostic procedure; if the abdomen becomes flat, he knows what type of bloating is present. Krukenberg used much the same technic in 1884.

It would seem that in pushing the abdominal contents forward, bloating should be facilitated by the simultaneous relaxation of the muscles of the anterior abdominal wall. Sometimes the muscles are relaxed, but sometimes they are contracted, tense and hard. In 1 case (reported by me in 1945 [22]), in which the syndrome was, I believe, a variant of the one described in this report, the patient's contracted, boardlike abdominal wall was always flat. Perhaps the flatness of the abdomen was due partly to the contraction of the muscles of the anterior abdominal wall, and partly to an absence of a forward thrust from the muscles at the back.

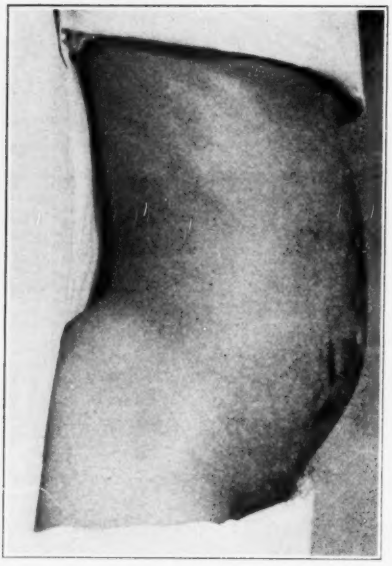

Fig. 3.—Lordosis producing the appearance of bloating. (From Bargen, Adson, Lundy and Dixon.[21])

That lordosis is not an essential factor in the bloating was obvious in some cases. For instance, lordosis does not appear to have had anything to do with the tremendous bloating of the woman whose abdomen was pictured by Vaughn [23] (fig. 7). She bloated when her hand was placed in ice water, and the abdomen deflated when the hand was

22. Alvarez, W. C.: A Rare Syndrome of Crisislike Abdominal Pain, Gastroenterology, **4**:296, 1945.

23. Vaughan, W. T.: Practice of Allergy, St. Louis, C. V. Mosby Company, 1939.

warmed again. Long ago Simpson [4] noted that in some cases lordosis was not a factor.

Significance of Contractions or Bloating of a Part of the Abdominal Wall.—A feature which helped convince me that this syndrome is due primarily to spasm of the muscles of the abdominal wall was the observation of several cases in which the bloating, like a phantom tumor, involved only half the patient's abdomen, or even only one quadrant of it.

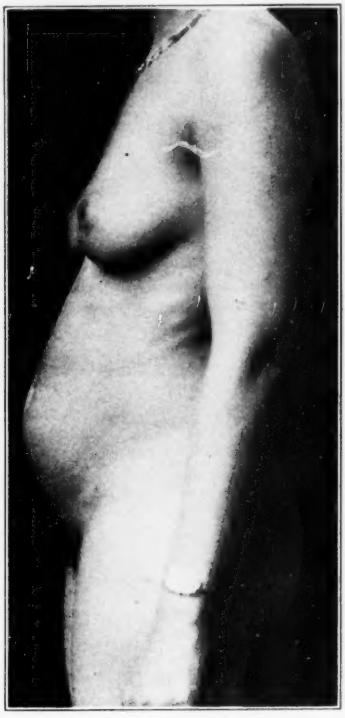

Fig. 4.—A slightly bloated woman, with some lordosis.

In 1 case, the bloating would begin in the left lower quadrant. Then, by bending and twisting in a certain way, the patient could, as she said, "throw the tumor over" into the right lower quadrant; it might then suddenly disappear. I saw her one day when she was bloated only in the right lower quadrant. Two women bloated only on the right side, with a contraction of the abdominal muscles on that side; one day I watched 1 of them as she bloated on only the left side. One woman

bloated only in the upper half of the abdomen and 1, only in the lower half. Another would bloat first above the navel; the swelling would then spread into the lower half of the abdomen. Swelling in the case of another woman would begin with a contraction of the abdominal muscles in the left upper quadrant; the patient then would bloat over the entire abdomen.

In a few instances, segments of only one rectus abdominis muscle would go into spasm to such a degree that some physicians who saw the patients thought they were dealing with a tumor. A nervous man with this condition was one day rushed to a hospital by his surgeon for removal of a supposed cancer of the cecum. Fortunately, the man's brother insisted on a consultation. When I first saw the patient, the tumor was obviously in the lower half of the right rectus muscle, but

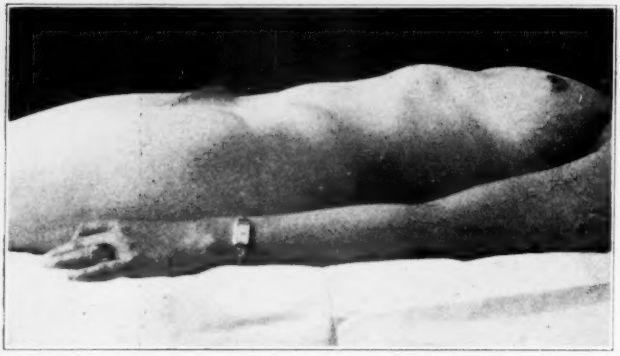

Fig. 5.—The woman of figure 4, lying down. The bloating has suddenly disappeared.

when I doubled him up, it disappeared for good. One of the women whose case is described in this report had a similar "tumor" in the lower half of the left rectus muscle. In the case of another bloater, a man, the wife noted that at times there were "knots" in the right rectus muscle. In the case of 1 woman bloater, the anterior abdominal wall would suddenly become tense and then relax, and it is probably highly significant that in 3 other cases, with the bloating and the cramping of the abdominal muscles, the women had cramps also in the muscles of the arms and legs or of the thoracic wall. Seventy years ago, Mitchell [5] saw bloaters with these "small phantom tumors" of the pectoral and other muscles. Talma,[12] in 1886, commented on one-sided bloating.

In 1 of my cases, the woman suffered for years from cramps in her thigh and abdominal muscles, so sudden and severe that they often threw her to the ground or caused her to fall downstairs. Such falls raised

the question of possible epilepsy, but she said that she never lost consciousness. At night, the spasms would cause a knee to jerk painfully up to her chin and would wake her, screaming. She said that when she was bloated, her arms and legs would stiffen.

In another case, the woman, when beginning to bloat, felt a sensation of spasm traveling up the esophagus to the throat. Another, during the spells, would have some trouble swallowing solid food, indicating spasm

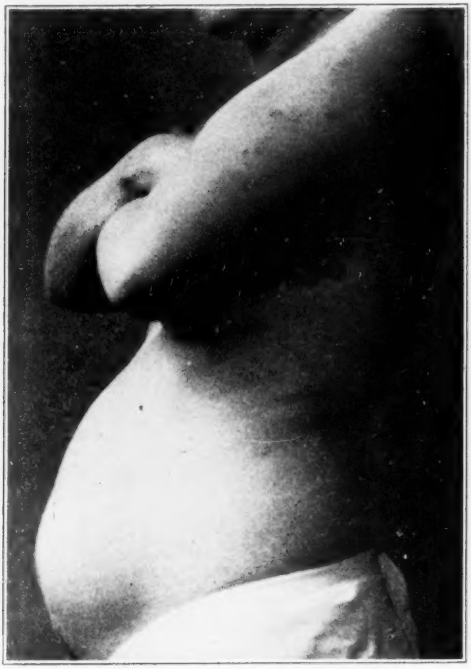

Fig. 6.—A bloater slumped into her usual posture.

of the esophagus. Two other patients experienced painful cramping of the rectum or of the anal sphincter. In another case, just before bloating began, the patient would feel something snap or "block" in the right lower quadrant of the abdomen; the whole abdomen would then become so sore that it hurt her to walk. One woman said that at the beginning of a spell she felt as though a band were tightening in her epigastrium. Perhaps highly significant of a psychic cause for the phenomenon is the fact that 1 woman felt as if a hand were grasping the anterior abdominal wall and pulling it forward.

Osler [20] and a number of other writers on the subject of bloating noted the contractions of the rectus abdominis muscles. Haultain [16] said that he saw sudden bloating in 2 cases of patients with an obviously relaxed abdominal wall; 1 was a man who had just been subjected to paracentesis and the other, a woman who had just had a large ovarian cyst removed. One coughed violently, and the other vomited; in each

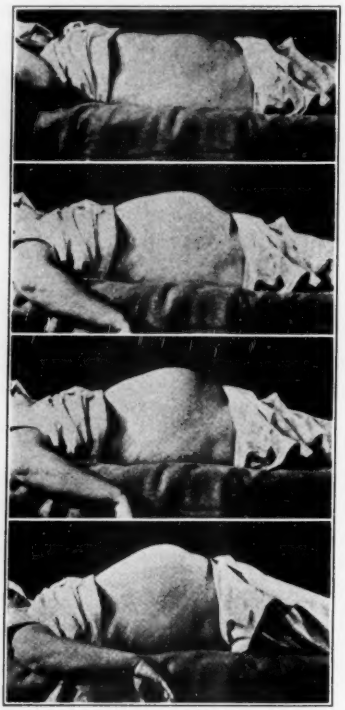

Fig. 7.—Several stages in the rapid bloating which took place when a woman's hand was placed in ice water. (From Vaughan.[23])

case, with the accompanying spasms of the abdominal muscles, the patient bloated.

Some horses bloat in an effort to avoid having a saddle girth cinched tightly. They probably do this by contracting the abdominal muscles.

The Diaphragm.—For a time I suspected that the bloating was due to a pronounced descent of the diaphragm, and in a few cases, while watching with the roentgenoscope, I saw this action taking place. The

diaphragm dropped to its lowest possible position, and its movements then became shallow and irregular. In other cases, however, the diaphragm was up in its normal position when observed. Contrary to the theory that a considerable descent of the diaphragm was the main cause of the bloating was the observation that no matter how deep a breath some patients might take, they could not produce the typical bloating. Interestingly, one woman's attacks of bloating began with

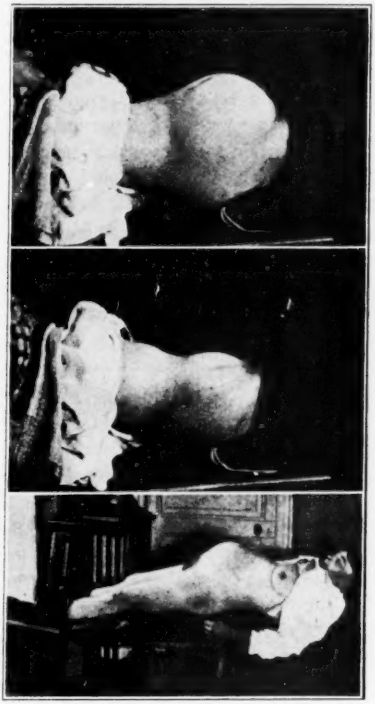

Fig. 8.—Top, a girl when bloated; center, the same girl after she had obeyed the command to deflate. Bottom, another bloater. (From Kaplan.[3])

hiccup and another's with sneezing, which suggested involvement of the diaphragm. Talma mentioned a bloater whose condition became worse when he was hiccuping. Kaplan's photographs show how, in some bloaters, the abdominal contents are pushed caudad (fig. 8).

The fact that in a few cases the diaphragm, with its cervical innervation so far orad to that of the other abdominal muscles, joined in the spasm, indicated that the storm causing all the contractions was arising

in the brain. One wonders whether, perhaps, spasms in the diaphragm, brought on by emotion, often caused the ancients to use the same word for the diaphragm as for the brain. Some modern words, such as "frenzy" or "schizophrenia," have such an origin.

Osler,[20] who knew bloaters, stated the belief that the distention must be due largely to spasm of the diaphragm, and a similar view was held by Talma,[12] Da Costa,[14] Gowers,[9] Kerr and Ferguson,[17] and others. Simpson [4] said that he could sometimes make bloating disappear by relaxing a patient's diaphragm. He did this by having the woman take a deep breath and then exhale, or by having her count aloud as long as she could without taking a breath.

Several Mechanisms.—As I have already admitted, in some cases, especially when there was no pronounced lordosis or no considerable flattening of the abdomen when the patient lay down, I was at a loss to explain the mechanism which produced the bloating. As Kausch,[24] Fitz [25] and others said long ago, there must be several ways in which a neurotic woman can make her abdomen bulge forward. I can only be certain that in most cases described in the present report, the bloating was not due to any increase in the bulk of the intestinal contents.

Kaplan's photographs (fig. 8) suggest that there is something in Schatz' contention (1872) that when much pressure is put on the contents of the abdomen, as on a balloon, it tends to assume a globular form.

THE TYPE OF PERSON WHO BLOATS NERVOUSLY

In the present series of 92 cases, there were 85 women and 7 men. This sex distribution alone indicates a functional origin for the disease, because organic diseases of the abdomen, with few exceptions, involve 3 or 4 men to 1 woman. Eighteen of the women were unmarried (an abnormal proportion), and most of these were too psychopathic or undersexed ever to marry. Few of them had ever gone out much with men; one said that she never wanted to go out with men; several had no sexual feeling, and one was a nun who was said by her Mother Superior to be "a bit difficult."

Seven of the women who had married had been divorced, and at least 22 of those who were still married were unhappy, or had made a poor sexual adjustment. Four remarked that they had made a mistake in marrying a man too old for them; 1 had married a dipsomaniac. One, who had married at 17, was still a virgin at 55! She said that her

24. Kausch, W.: Beiträge zur Hysterie in der Chirurgie, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **17**:469, 1907.

25. Fitz, R. H.: The Relation of Idiopathic Dilatation of the Colon to Phantom Tumor, and the Appropriate Treatment of Suitable Cases of These Affections by Resection of the Sigmoid Flexure, Am. J. M. Sc. **118**:125, 1899.

husband's few early attempts at intercourse had caused her so much pain and disgust that thereafter he had left her alone. She had a toxic goiter, and her 2 sisters, also goitrous, were queer "old maids."

The most frequent comment in my notes as to the personalities of the women bloaters was "very nervous." Many were described as "constitutionally inadequate" and always ailing; shy, with a negative or schizoid personality, or very sensitive and worrisome, tense, irritable, often tired, sometimes depressed, psychopathic, and inclined to cry without apparent cause. At least 16 were unstable and had had one or more nervous breakdowns or mild depressions. Two had been mildly manic at times, and 2 had attempted suicide. One had been in a psychopathic hospital. Three confessed to an almost insane temper; 3 had had spells of anorexia nervosa; 1 patient said that she was a "screwball"; 3 had low intelligence; several were often jittery, excitable and shaky; several feared that they were going insane; others jerked and feared a convulsion; some had feelings of confusion, or of being drugged, and others had severe claustrophobia. Two said that they had had an unhappy childhood because of mean parents, and many were most unhappy and full of grief when I saw them. Two had much strain and sorrow because of mentally defective children.

Several patients tended to hyperventilate when nervous; others suffered from palpitation or spells of smothering; several fainted easily; 1 had facial tics; several got dizzy easily, and 1 salivated at times. Some had terrible nightmares; many fretted a great deal; 1 as a girl had been stricken with diarrhea whenever a beau came to visit her. Some said that they had pains all over their bodies; 1 was a chronic follower of quacks of all kinds; several had nerves that played tricks with them all the time; 1 suffered from neurodermatitis; some had air hunger at night; 1 had had chorea; some reacted adversely and violently to drugs, a sign of a nervous makeup. Evidently, most of these patients were anything but normal neurologically.

Menstruation.—As is often the case with psychopathic women, at least 14 suffered from dysmenorrhea and some, from severe premenstrual tension. Seven mentioned a scanty flow. At least 2 mentioned flooding. For no detectable reason, 1 stopped menstruating at the age of 21, and several submitted early in life to hysterectomy. Several had a male distribution of body hair, suggesting poor ovarian function.

Appearance of the Patient.—In spite of the high percentage of psychopathic and neurotic persons in the group, I noted comments, on the history sheets, indicating that 13 were pleasant persons and that several were lovely, attractive, well built women who looked well. Indicating neurosis was the fact that in spite of much suffering, at least 11 were overweight. Only a few were too thin.

Hysteria.—Many of the women, while under observation, had hysterical episodes, with such symptoms as paralysis, aphonia, shuffling gait, locking jaws, queer, overemotional behavior or attacks of severe air hunger. A dozen others told of hysterical attacks, with "unconsciousness" lasting several hours. Five gave a history of illnesses which had been considered episodes of encephalitis, but which sounded to me more like prolonged attacks of major hysteria; none of the episodes had left any residue of parkinsonism. A few patients were reacting badly to a physical handicap, as in the case of a woman who was an achondroplastic dwarf and that of a man who was born without one ear and with only half the mandible.

Hypersensitiveness.—Many patients were of the hypersensitive type; 1 said that whenever she was to start on a journey, she would lie awake all night and would urinate every fifteen minutes on the day of the trip. Several had an irritable bowel syndrome, with the formation of much mucus. Several patients, with a normal heart and thyroid gland, had a pulse rate between 120 and 140 beats per minute when first interviewed; later the rate became almost normal. Some had submitted to thyroidectomy without obtaining relief.

One woman was so hypersensitive that she could not stand a simple rectal examination. Most patients had greatly exaggerated deep reflexes. In 1, the knee jerk was so strong that the leg on the other side jumped too. When I touched a trigger zone on 1 woman's back, she belched repeatedly.

Racial Stocks.—No particular racial stock seemed to predominate in this group of patients.

Migrane.—At least 32 of the 92 women suffered, or had suffered, from migraine. This incidence is higher than that in the clientele which I see usually and would suggest that some relation exists between the migraine and the bloating. Actually, all but 2 of the patients with migraine said that they could see no relation between the headaches and the bloating. In a few cases, the headaches had almost stopped before the bloating became a problem. In 1 case, however, many of the attacks suggested an equivalent in migraine.

The impression I gained was that the migraine only made the patients more sensitive and sickly, and therefore more inclined to bloat. Contrary to the idea that the present form of bloating is an equivalent of migraine is the fact that in 2 cases, the episodes continued during several pregnancies; in another case, however, the woman was free from bloating during pregnancy. Additional evidence against migraine as a cause of bloating was the fact that injections of ergotamine tartrate U. S. P. (gynergen®) did not improve the condition.

REPORT OF CASES OF BLOATING IN MEN

Because there were so few men with the syndrome it is of interest to scrutinize their cases to see what sort of human beings they were.

CASE 1.—A painter of 45 was a sullen, nervous, intense man, much of whose history was typically that of a "relative of the epileptic." He was so irritable that he avoided arguments, for fear he might attack and kill his adversary. He bloated suddenly when he became excited or angry; sometimes the distention woke him out of sleep. He did not dare eat with friends, for fear he would bloat after taking a few mouthfuls of food, and he would not even permit his wife to be with him at table. As was to be expected, his first wife had left him and his second was about ready to do so.

When bloated he would salivate. He would get up, walk around and rub his abdomen until he would belch explosively, thus obtaining some relief. His tendency to bloat had appeared twenty years before, after a drinking bout. Somewhat contrary to my theory that the patient was a "relative of the epileptic" were the lack of a family history of the disease and a fairly normal electroencephalogram. Aside from the irritability and bloating the patient was strong and well.

CASE 2.—A worrisome clerk of 49 began to bloat when a physician sent him into a panic by telling him that he would have to have his appendix out. With the bloating, severe globus hystericus occurred. The patient appeared to be a typical bloater, with no flatus.

CASE 3.—A not-too-successful attorney of 36 had a deforming facial defect, which handicapped him and caused much mental suffering. His bloating seemed to be typically nervous in type.

CASE 4.—A big, husky farmer of 61 appeared to bloat typically; relief occurred with a gurgle. He had the usually neurotic "hurting" of one-half the body, from head to foot.

CASE 5.—A man of 47 had lifted himself by hard work from a job as a mechanic to that of service manager of a large corporation. He had three phones clanging on his desk from 7 a. m. until midnight. For ten years he had had spells in which he would get tense and then bloat. A little whiskey would bring prompt relief. In the spells, the right side of the abdomen became rigid. The patient smoked three packages of cigarets a day. He had a deformed duodenal cap, but no symptoms of ulcer.

CASE 6.—A small, depressed-looking, nervous, constitutionally inadequate stock clerk of 58 had typical bloating after eating, annoyance or exertion, such as that needed for mowing the lawn. "Knots" developed in his rectus muscles, which were relieved by his doubling up or lying down. He was mildly manic-depressive in temperament. He had been bloating for twenty-seven years. He complained also of smothering spells and hot flushes.

CASE 7.—A stocky, muscular, cheerful, middle-aged man, with poor nervous heredity and unhappiness in his home, bloated frequently. Hypersensitivity of the abdominal autonomic nerves was indicated by the fact that urination brought abdominal cramps and a feeling that diarrhea was impending.

SIGNS AND SYMPTOMS

Heredity.—Doubtless highly significant is the fact that in 16 of the 92 cases, a history of insane ancestors was recorded. In 9 more cases, there was a history of epilepsy in near relatives; in 2 cases, the women

had defective children. Thus in 30 per cent of the patients there was a strong suspicion of poor nervous heredity. It may be significant that 7 patients had relatives with diabetes, and that 3 had relatives with toxic goiter. One woman's mother bloated. Many relatives had migraine and were allergic.

Age Incidence.—Most of the 92 patients were in their thirties and forties when first seen; 9 were in their twenties, and 11 in their fifties.

Onset of the Disease.—In 3 cases, the disease had begun in childhood and in 1, after measles. In several, it had begun when the patient was 16 or 17 (perhaps with the excitement of graduation). In some cases, the bloating had appeared for the first time shortly after an early and unhappy marriage, while in others it had followed an operation, a miscarriage, the death of both parents in an accident, an attack of severe indigestion, an episode of vomiting or diarrhea, an unexplained fever, a period of overwork or a child's first epileptic convulsion. One woman had begun to bloat when her maid left her; 1, when a maid stole her mink coat; 1, when she discovered her husband's infidelity; 1, after her marriage to a dipsomaniac; 1, while helping in an election campaign; 1, when her mother committed suicide, and 1 when, at Christmas time, she overate and took a cathartic for relief.

Another patient, a temperamental young woman, married a dashing fellow, found that she had gonorrhea and divorced the man; then, still much in love, she arranged for remarriage, only to find, a few days later, that the man had eloped with another woman! After unhappy experiences with another man, the woman began to bloat. Another woman began to bloat when she too found that she had acquired gonorrhea from her husband. One woman dated her illness from the mental shock of discovering at 28 that a surgeon had tied her fallopian tubes at operation. She had experienced a few months of overcompensation with nymphomania and then had become sexually anesthetic and had begun to bloat. In several cases, the woman was in love with a married man who was not free to marry her.

Exciting Causes of Individual Attacks.—Many of the bloaters knew that the attacks were likely to accompany any excitement, pleasant or unpleasant; any argument or fright; much standing or walking; hard horseback riding, or anything that produced fatigue. One woman said that she bloated whenever she "got to feeling ugly." One bloated when frightened about her boy's attacks of asthma; other patients bloated when they became angry, or when they were hurt in any way, mentally or physically. Some had most difficulty when distressed by hot weather; some, when worried or tired after a sleepless night. The very nervous wife of a doctor bloated whenever her husband was called out at night leaving her alone in the house. One woman bloated whenever she

fussed over her husband's coming late to supper and another, when her husband complained about her cooking. Another began to bloat when she tried to break away from a domineering sister.

Most patients had found that any large meal, particularly supper, was likely to produce the distention. As a corollary of this factor, many patients remained fairly well when they ate but little. Some found that they could safely plan to go out in the evening if they would eat nothing at all during the day. One, however, on one occasion fasted for three days and still was bloated.

In some cases, constipation was an exciting factor, but it was not the only or the essential one, as shown by the fact that often when the bowels were moving well or the colon was kept clean with enemas, the women still bloated. Some patients even said that they dreaded a bowel movement or the taking of an enema, which might act as a trigger mechanism and start the bloating. Some said that they would be well if only they could do without defecation. In 7 cases, enemas helped a bit in averting the spells; however, enemas rarely helped much during an episode; 1 woman took three a day and still remained bloated. Others took a daily cathartic and were the worse for it.

A few patients would experience bloating when they sat bent over forward. For that reason, 1 could not pick berries, and another could not sit hunched over in a boat, fishing.

Effects of Menstruation.—Curiously, in the cases of the women, only 10 said that menstruation was a factor in bringing on attacks. In the cases of 2 of the more psychopathic women, the bloating was associated with premenstrual tension.

Time of Day.—About equal numbers of the patients experienced bloating before daybreak (waking them), before breakfast, after breakfast, after supper and in the evening. Most of them said that the distention appeared during the afternoon, or within a few minutes after any large meal. Some said that the bloating might come at any time; others said that it never came in the early morning. Many said that they usually awoke feeling well in the morning.

Length of Episodes.—The great majority of women said that the bloating almost always disappeared overnight. Eleven women said that an attack might last from two to four days, and a few others said it might last one or two weeks.

Condition of the Abdomen.—In some cases, the patient's abdomen was as tense as a basketball, while in others, it was fairly soft. In the office, a woman might have a tense abdomen one minute, while the next minute it would be relaxed. Usually the percussion note was not unusually tympanic. Often the abdomen was not tender to the touch. In most cases, the patient did not seem ill.

Pain or Discomfort.—Many women spoke of discomfort, misery, aching, distress, hurting, burning, gnawing or of a feeling of distention, pressure or bursting, when bloated. A few had pain so severe that they walked the floor groaning, grunting or grinding the teeth. A few behaved like a woman in labor, with pains coming every four or five minutes. Because of this suffering, at least 2 of the women became habituated to morphine and several were in danger of this. In most cases the pain was constant, but in a few it was rhythmic; 11 women spoke of cramps. A few thought that the pain arose in the contracted muscles of the abdominal wall. As one would expect, because of the forced lordosis, a few had backache during spells. In some cases, there was pain only during some years of the illness, or during certain attacks. One patient said that pain "ran up into the head." Only 2 mentioned soreness of the abdomen. Five said that they would get sore all over. Some were so sore that they liked, during spells, to lie on the side with the knees drawn up. When in a crowd, they were much afraid of being jostled.

Twenty patients said that they had little, if any, discomfort. These complained only of their appearance, which, especially in the case of an unmarried woman, was embarrassing. In some cases the woman was too ashamed to go out in public, and in a few her appearance interferred with her holding a beau. One said that her friends amused themselves by watching her bloat after a meal.

Location: In 5 cases, the pain began or stayed in the upper half of the patient's abdomen; in 3 each, it was in the left half or the right lower quadrant. In 1 case, it was in the left lower quadrant. In 1 each, it was in the right upper quadrant, the lower half, the right half or all over the abdomen, up into the thorax. In the case of 1 woman, it often closely resembled the pain of gallstone colic, but cholecystectomy did not help.

Peristalsis.—The pain, when present, did not appear to be arising in contractions of the bowel, because of the quietness of the abdomen. In only a few cases was there any borborygmus during a spell, and in only 1 case was there ever any visible peristalsis; this did not occur during bloating. Most patients said that while they were bloated they had no desire to move the bowels and never passed gas. Most of them could eat and digest while bloated; in only 2 cases was gastric stagnation noted. In these 2, roentgenologic study showed neither a pyloric lesion nor pyloric spasm to explain the stasis.

Terminal Gurgle.—Interestingly, several patients stated that a few moments before the swelling receded they would hear a gurgle in the upper part of the abdomen or on the right side. One woman would hear this gurgle after taking morphine, which would stop the bloating.

Another woman, after hours of suffering, would say, "Here's the gurgle; it's going to let go," and in a few seconds she would be relieved. This feature suggests that some center in the nervous system not only causes the abdominal muscles to contract but also stops movements of the bowel. When the "storm" in the center lets up, the bowel apparently relaxes first, allowing a bubble of gas to move caudad. The terminal gurgle appeared in 1 case only after the taking of a big dose of atropine, perhaps with some morphine.

Some of the women noticed a large flow of urine at the end of an attack, such as is seen in some spells of migraine.

Other Symptoms.—Twenty-five of the women complained of nausea, and in 6 cases, the symptom was severe. Seventeen vomited during certain spells. Three induced vomiting, in an effort to get relief. One had sudden, uncontrollable spells of projectile vomiting, even with an empty stomach. Some recovered from the vomiting with the passage of time. At least 15 were subject to attacks of belching; 3 of these were accomplished air swallowers. Seven spoke of mucous colic and 3 of heartburn. Ten regurgitated food soon after eating, always a nervous habit. Seventeen had an occasional attack of diarrhea, almost always between spells. Several had a headache when the spell lasted a long time. At least 28 of the women were constipated. Five complained of dizziness, with or without bloating. Some got week in the knees during spells and were unable to stand. Four patients commented on an occasional rather sudden loss of from 20 to 40 pounds (9 to 18 Kg.) in weight.

Other seldom mentioned symptoms were a feeling of interference with breathing, profuse sweating, a feeling of being dazed, quivering and the advent of bad breath. Only 1 stressed occasional fever.

ADDITIONAL FACTORS

Relation of the Disease to a Trigger in the Digestive Tract.—It is important to note that most of the patients with this disease had an excellent or fair digestion, not only between the attacks, but even during them; in other words, the indication was that the bloating was not due to indigestion or to any lesion in the digestive tract. This agrees with the fact that in almost all cases, repeated roentgenologic studies and abdominal explorations had failed to show any significant lesion. In the 3 cases in which the gallbladder was probably diseased and was removed, the bloating returned sooner or later, unchanged. In a few cases, the disease actually began after the removal of the gallbladder or the appendix. In all but 10 cases, the person was unusually free from abdominal gas and from the need for passing flatus; only 4 occasionally got some relief by passing gas.

The fact that a number of patients would bloat as soon as they started chewing one mouthful of food, or after drinking a glass of cold water, taking an enema or defecating, suggested strongly that the digestive tract contained triggers that could, in a purely mechanical way, start a train of reflexes. The condition may be like that in tabes dorsalis, in which, as Foerster [26] once pointed out, eating can serve as a trigger to start a gastric crisis.

Allergy.—Allergic sensitiveness appeared to aggravate the situation in at least 25 cases. In 14 cases, the patient was sure that the nature of the food eaten had no effect on the bloating. In many, an elimination diet did no good. In only 4 was it decidedly helpful; 2 women said that they could stay well as long as they ate only meat or cottage cheese. Four patients were asthmatic, 2 had hay fever and 3 had urticaria. Others showed no sign or symptom of allergy.

The suddenness with which most patients bloated after a meal was evidence against an allergic mechanism: There was hardly time for it to act.

Coexistent Conditions.—A few patients had conditions or histories which were probably only coincidental, because they were not present in the other cases. I refer to mild hypertension in 7 cases, paroxysmal tachycardia in 2, extrasystole in 2, a primary type of anemia in 2, the resection of a segment of bowel in childhood in 2, pruritus vulvae in 2, a scar of an old duodenal ulcer in 2 and a pseudoulcer type of syndrome in 4. A few had a small, nontoxic adenoma of the thyroid gland. Several had no free hydrochloric acid in the stomach.

Negative Results of Examinations.—In the present paper, space is not given to reports of the careful medical examinations made because, in every case, they failed to yield any positive or significant findings. The blood pressure was almost always normal. In all cases, the patient's stomach, gallbladder and colon had previously been well studied roentgenologically; the organs were usually studied again at the Mayo Clinic, with negative results. In a few cases, the small bowel was carefully studied roentgenologically and was shown to be free of any obstruction. In several cases, the function of the liver was studied, and no retention of dye was found. In some cases neurologic studies were made, which showed nothing significant. In the few cases in which the spinal fluid was examined, it was normal. Electroencephalograms were essentially normal in 3 cases and showed dysrhythmia in 2; in these 2 cases, the bloating may have been an epilepsy equivalent. As already noted, in most cases the patient's

26. Foerster, O.: Die Leitungsbahnen des Schmerzgefühls und die chirurgische Behandlung der Schmerzzustände, Sonderbände zu Bruns' Beiträgen zur klinischen Chirurgie, Berlin, Urban & Schwarzenberg, 1927.

abdominal cavity had been explored repeatedly, with essentially negative findings.

Efforts to Avoid Bloating.—No good method has been found for avoiding the attacks. Some women had fewer spells when they avoided fatigue, exercise, annoyance, conflict, loss of temper and overeating. Four were almost well when they stopped working and took a rest. Four were much better when they stayed in bed. Two were all right if they lived on meat or cottage cheese, and 17 were much better if they ate very little. Four were helped by wearing a tight girdle. One could prevent an attack by taking an injection of estrone U. S. P. (theelin*); however, I tried this treatment on a few women, and only 2 obtained even slight benefit. Two said they could avoid attacks by taking laxatives, and 7 were somewhat better for the taking of enemas. On the other hand, 1 woman said that she could avoid attacks by restraining defecation for days.

Some of the women might have recovered if they could have got rid of a bad husband and found a good one. Some might have been cured by a good annuity. Others might have been helped by a psychiatrist. In a few cases, an elimination diet helped. A few women could have helped themselves by reducing weight: They would have had a much smaller abdomen.

In most cases, bromides and barbiturates had been tried without avail. Krukenberg's patient was helped by wearing a back brace, which combated the tendency to lordosis.

Uselessness of Operations.—As already noted, most of the women had been operated on many times, with no permanent relief. Happily, some twenty years ago we at the Mayo Clinic learned never even to explore the abdomen of these patients.

Following is a list of the operations submitted to by 1 woman between 1929 and 1941: Appendectomy, abdominal exploration, removal of an ovarian cyst, cholecystectomy, removal of adhesions, thyroidectomy, removal of a big toe, resection of a segment of the small bowel, removal of the coccyx, curettage and left mastectomy. Another woman had, in succession, appendectomy, suspension of the uterus, removal of an ovary, lumbar sympathectomy, cholecystectomy and removal of adhesions. One had, in nine years, salpingectomy, right ovariectomy, left ovariectomy, drainage for postoperative peritonitis, removal of adhesions and suturing of the right kidney; in one period of fourteen months, she was hospitalized five times. These are not unusual records for bloaters. As will be noted, some of these women get themselves operated on not only for bloating but for other troubles, such as a sore coccyx. This practice throws light on their temperament.

The point to be noted by all surgeons is that every one of the operations performed in these 92 cases with the hope of curing the bloating was without result. Even in the few cases in which gallstones

were found and removed, the bloating went on as before. The reason for this 100 per cent failure of surgical intervention would appear to be that in this disease the cause is never in the abdomen.

Another important point for the surgeon to remember is that if on anesthetizing a bloater in an acute attack the abdomen should become flat, the proposed operation should be called off; the diagnosis of functional bloating will have become obvious. The importance of this observation was stressed by McDonnell [13] as long ago as 1855.

As yet, even some eminent surgeons do not recognize this disease and do not know the futility of operating in an attempt to find the cause of it. At the time of writing, 1 of the highly neurotic women whose case is reported here has just had her sixth operation at the hands of one of America's leading surgeons. Since her basic trouble is that she married an old man whom she hates to live with, she is still bloating.

Efforts to Terminate Bloating.—The treatment of attacks is unsatisfactory. At least 17 of the patients said that the only way to obtain relief was to lie down and rest. Three said that they could get some relief by violent belching; 2, by washing out the stomach, and 2, by eating some food.

At least 9 knew that an injection of morphine, dihydromorphinone hydrochloride U. S. P. (dilaudid hydrochloride®), meperidine hydrochloride (demerol hydrochloride®) or codeine would relieve them. All that saved some from habituation was the fact that morphine made them very ill. One continued to bloat even when she was taking 1½ grains (0.1 Gm.) of morphine each day; the drug only lessened her pain. A few patients were not helped much by morphine: The abdomen would not become flat when it was used. One woman was helped by an injection of posterior pituitary injection U. S. P. (pituitrin®) which made her bowels move, but the case was atypical. Another woman tried the same drug without avail. Many other drugs, such as epinephrine, belladonna extract, atropine, benzyl benzoate, alcohol, amyl nitrite and histamine phosphate, were tried repeatedly without result. One man got good relief with whiskey, but a woman who tried it only became more nauseated. One woman could get prompt relief from an intravenous injection of pentobarbital sodium U. S. P., but in several cases, barbiturates only made the patient "wild." Only 1 woman said that she got some help from injections of gynergen.® In my hands, gynergen® and dihydroergotamine tartrate (DHE 45®) did not help bloaters. One patient got some help from neostigmine methylsulfate U. S. P. In bad attacks with much vomiting, a 3 grain (0.2 Gm.) rectal suppository of pentobarbital sodium U. S. P. or an intramuscular injection of 3 or 7½ grains (0.2 or 0.45 Gm.) of amobarbital (amytal®) sometimes helped. Two patients would take some bicarbonate of soda and belch. In some cases enemas helped to calm

an attack, but in most cases they were of no help; in 3 cases, they made matters worse.

In Goldschmidt's case,[6] splanchnic anesthesia did not help, and the administration of epinephrine made the girl worse. Her abdomen would become flat after an injection of ergotamine tartrate or afenil® (a molecular compound of calcium chloride and urea), but soon she would bloat again. In the case reported by Bargen, Adson, Lundy and Dixon,[21] splanchnic block caused the bloating to disappear. It is said that Janet could sometimes stop an attack by "suggestion." Kaplan said that his teacher, Bernheim, could make a bloated woman's abdomen become flat by ordering her to stop bloating. Several early writers told of stopping an attack by exerting steady manual pressure on the distended abdomen.

USUAL COURSE OF THE DISEASE

Because I saw most patients in consultation and then seldom heard from them again, I cannot say much about their subsequent histories. Only 1 of the women lived near enough so that I could observe her progress through the years. She largely recovered from the bloating when she adjusted fairly well to an unhappy domestic situation, but at the time of this report she still has one nervous trouble after another.

Another woman stopped bloating but is still a nervous complainer. Highly informative is the fact that a woman who had bloated severely, and who had been incapacitated by this disease for half a lifetime, recovered when her dipsomanic husband died; since his death she has been happily at work in a store. Another patient, seen after an interval of ten years, was still bloating; others had had several more operations and had been hospitalized several times for morphinism. A few others reported after some years that they were better, but still bloating occasionally. That the disease is often long lasting and fairly hopeless can be seen from the fact that when I first saw some patients, the condition had been recurrent for ten, twenty or thirty years.

In the worst cases, and especially when there is a large element of psychopathy, with low intelligence, or a bad domestic situation with constant strain, unhappiness and frustration, the prognosis is bad, and I know of nothing likely to help. The woman continues to go from one clinic or physician to another, wasting large amounts of medical time and often large amounts of the charity funds available in her city.

Unfortunately, most of the women I have heard from were having more useless operations. One wrote me that after the usual series of appendectomy, cholecystectomy, partial hysterectomy and operations for adhesions, she had had lumbar sympathectomy, left phrenicotomy and bilateral splanchnicectomy. The appearance of her abdomen years ago, when I first knew her, is shown in figure 9. When last I heard

from her she was no better, though she thought that the sympathectomy might have stopped the vomiting during bloating. Her real trouble, I think, was that she was in love with a married man. Another woman reported that an abdominal sympathectomy had failed to give relief.

One woman returned years after examination to say that she had been cured miraculously by a chiropodist, who had placed a pad under the anterior end of her os calcis to tip it up!

Fig. 9.—Typical scarred abdomen of a bad bloater.

EARLY STUDIES OF THIS AND RELATED DISEASES

The earliest report I found of a phantom tumor in a hysterical girl was that by Bright.[27] Even in the preanesthetic and preaseptic days of 1824, this girl had already had two futile abdominal explorations when Bright saw her!

27. Bright, R.: Hysterical Distention of the Bowels, Mistaken for Ovarian Tumor: Operation to Attempt Its Removal, Guy's Hosp. Rep. **3**:257, 1838.

O'Donnell, in 1855, and Priestley, in 1858, showed that by giving chloroform one could diagnose hysterical bloating. In 1871, Cadet described a case of hysterical bloating in which the spell lasted several days. Kaplan stated that in 1872, Wells described and pictured cases of nervous bloating.

In 1881, Mitchell described a patient with nervous bloating whom he had seen some twenty years before. The patient was a woman whose life had been embittered by marriage to a worthless man. After losing all her money, she began to have spells of pronounced enlargement of the abdomen, due not to flatulence but to painful emotion. Mitchell learned years later that she had gradually got well. He saw another patient in whom any handling of the anterior abdominal wall would cause the muscles to contract, producing a phantom tumor.[28]

Krukenberg's description of the disease, made in 1884, is good, and Kaplan's thesis on the subject, published in 1900, is excellent; he briefly reported 18 typical cases, collected mainly from the literature. Kaplan, and later Kausch, gave a good introduction to the older literature on the subject of the hysterical abdomen. Kaplan stated that in some cases, the diaphragm descended considerably; in 1, the bloating was on only one side.

Zeckendorf,[29] in 1883, reported what were probably 2 typical cases, but he did not understand the problem so well as Kaplan.

In 1922, Goldschmidt [6] described a typical case of severe, painless bloating, the patient having a tense abdominal wall and no gas. A woman of 22, who was at times hysterical, was operated on four times in one year for what was thought to be intestinal obstruction. Each time the surgeons could find only an empty, contracted bowel. As soon as she left Goldschmidt's care she had another laparotomy; she continued to bloat for years.

In 1931, Christianson and Bargen [1] reported 5 cases of nervous bloating associated with obstipation and pseudoileus, and in 1936, Bargen, Adson, Lundy and Dixon [21] described the case of a hysterical woman who was a bad bloater. Their picture of her (fig. 3) shows the pronounced lordosis and the way in which it pushed the abdomen forward. She maintained the lordosis even when lying down.

In 1945, I reported 2 curious cases,[22] 1 of severe bloating evidently due to spasm of the abdominal muscles, and the other apparently of hysterical contraction of the abdominal muscles without bloating. In the latter case, the powerful contraction of the muscles in the anterior abdominal wall kept the abdomen flat.

28. Mitchell, S. W., cited by McArdle and Kolipinski.[10]

29. Zeckendorf, E.: Ueber die Pathogenese der Bauchtympanie, nebst Beiträgen zur Lehre vom Stoffwechsel bei der Hysterie, Göttingen, L. Hofer, 1883.

McArdle and Kolipinski,[10] in 1886, Paddock,[30] in 1928 and Bivin and Klinger,[31] in 1937, summarized most of the literature on spurious pregnancy and phantom tumors.

According to Bivin and Klinger,[31] who collected reports of 427 cases of phantom pregnancy, Hippocrates reported 12 of them, but I have not been able to find the reference. This syndrome of pseudocyesis appears to be a variant of the bloating disease described in the present paper. In pseudocyesis, the woman thinks herself pregnant and may remain bloated for months. She may have morning nausea, amenorrhea, breast changes and what she thinks is quickening, and she may even appear to go into labor. Bodenheimer[32] reported the case of 1 of these women, who on several occasions was rushed to a hospital because she thought she was in labor. She finally became so well known to the admitting surgeon that he would send her home without even examining her!

SUMMARY

A syndrome is described, consisting of pronounced bloating, due not to gas, but to a contraction of the abdominal muscles and often to the assumption of a lordotic posture, which forces the abdomen forward. Commonly the swelling increases gradually during the afternoon and decreases at night, without the passage of gas. Occasionally the swelling appears so fast, or disappears so fast without the passage of flatus, that it is obvious that there could have been no change in the volume of the abdominal contents. Roentgenograms made of the bloated abdomen never show any excess of gas, and exploratory operations never reveal any physical cause for the syndrome. Even when diseased organs or a few adhesions are found, their removal does not produce a cure.

Ninety-two cases are reported, 85 of the patients being women and 7 men. Almost all were nervous, unhappy, neurotic or psychopathic. Many were relatives of insane persons or of those with epilepsy, migraine or diabetes. Most patients had good digestion between spells and sometimes even while bloated.

In these cases, the abdomen became flat a few seconds or minutes after (1) the induction of spinal or general anesthesia, (2) the blocking of the splanchnic nerves with procaine hydrochloride U. S. P., (3) the onset of vomiting, (4) the reception of an injection of morphine, or (5) the doubling up of the patient so as to alleviate the lordosis.

30. Paddock, R.: Spurious Pregnancy, Am. J. Obst. & Gynec. **16**:845, 1928.

31. Bivin, G. D., and Klinger, M. P.: Pseudocyesis, Bloomington, Ind., The Principia Press, 1937.

32. Bodenheimer, J. M.: Pseudocyesis, New Orleans M. & S. J. **81**:632, 1929.

Often the bloating appeared again as soon as the effect of a drug wore off, or as soon as the patient stood up and slumped.

Most patients lost much or all of the bloated appearances when they lay down, especially if the thighs were flexed on the abdomen.

In some cases, only part of the abdomen bloated, and only parts of the abdominal musculature became contracted. The diaphragm was sometimes involved.

The mechanism of the attacks appeared to vary somewhat in different patients, as did the symptoms. Some persons had pain, and others did not.

The nervous "storm" which produced the contraction of the abdominal muscles appeared to quiet the bowel, and in some cases, the attack terminated shortly after a gurgle was heard in the abdomen.

In many cases, an overly irritable digestive tract appeared to serve as a trigger zone, from which the bloating could be started. In such cases, a drink of water, defecation or the taking of an enema could start a spell.

Bloating often began after excitement, annoyance, fright or fatigue. Large meals also tended to cause bloating; some women could avoid it by going without food all day.

Physical, roentgenologic and laboratory examinations failed to show anything contributory.

No effective, safe way was found to terminate the attacks. Morphine will sometimes stop distress and flatten the abdomen, but the danger of using the drug is great; 2 of the patients became addicts. A suppository of pentobarbital sodium U. S. P. or an intramuscular injection of amobarbital sodium (amytal sodium®) may quiet the symptoms.

The prognosis for recovery is poor, but some patients recover when life becomes easier or happier.

No exploratory operation should be performed. If one is proposed during an acute attack and the swelling goes down during anesthetization, the diagnosis of functional bloating is made, and the operation should not be performed.

A review of the literature shows that nervous bloating has been observed for over a hundred years.

MEDICAL ASPECTS OF SUBMARINE WARFARE

The Human Factor As Reflected in War Patrol Reports

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ALTHOUGH World War II produced a tremendous volume of literature on many phases of military medicine, little information is available in the unclassified literature concerning the medical problems of submarine warfare. It is my purpose, in this paper, to discuss the problems in the light of personal experience and of material available in reports of submarine combat patrols.

During the war, American submarines made over fifteen hundred patrols. The commanding officers' reports of fourteen hundred and seventy-one patrols were available for study to evaluate the human factor in problems of combat. The conditions under which the reports were composed and the insignificance of medical details as compared with data relating more specifically to the mission of the submarines account for some inadequacies of this source of information. Commanding officers were not trained medical observers, and the emphasis which they placed on the human factor in combat depended largely on personal aptitudes and interests.

The fourteen hundred and seventy-one reports on which this paper is based cover patrols made from Dec. 7, 1941 to Aug. 14, 1945. The great preponderance of patrols were made in the Pacific theater, from Australian to Japanese and Arctic waters. The majority were carried out by the modern "fleet type" submarines; a relatively small number of patrols were made by the smaller and obsolete "S boats."

To understand the conditions under which submarine officers and men lived and fought, a description of conditions aboard the typical submarine on combat patrol is necessary. It was an existence characterized by extremely crowded living and sleeping conditions, limited

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water supply, frequent high temperatures emanating from the engine rooms and humidity resulting from the shutting down of ventilation during periods of contact with the enemy. Many missions were marked by days of fruitless patrolling and of almost unbearable monotony and boredom, sometimes broken by contact with the enemy, when excitement and tension were at a high pitch. Some patrols, though of short duration, were extremely active, the men remaining at battle stations for hours on end.

It is common knowledge that submarines are built compactly and that living arrangements are dictated by, and secondary to, military requirements. Sleeping accommodations were so limited that with an average-sized crew of about 75 it was always necessary for some of the men to share bunks by sleeping in shifts. Stowage space for personal gear was extremely limited. The only recreations possible were reading, card playing and listening to records. Once the submarine was under way, no one was allowed topside except the authorized watch. An active patrol often necessitated dawn to dusk submergence, with the the result that men did not see the sun for days at a time. While the ship was submerged, air within was cooled, freshened and recirculated by the air-conditioning units. Depletion of oxygen and accumulation of excess carbon dioxide sometimes occurred during periods of prolonged submergence. Though the supply of fresh water taken on at the start of the patrol was augmented by distillation, the total amount available was so small that showers frequently had to be limited. Condensate from the air-conditioning system was available for general cleaning, for use in the washing machine and sometimes for bathing.

Submarines had the deserved reputation of serving the best food in the Navy. However, the supply of fresh meat, vegetables and frozen foods was normally exhausted before the patrol was concluded, resulting in a monotonous diet the last few weeks.

The men and officers serving aboard submarines were carefully selected on the basis of high physical and psychologic requirements. Though a policy of frequent rotation to duty ashore was maintained, some men and officers accumulated an amazing number of war patrols on their record.

No physicians were assigned to duty on submarines in World War II, their place being taken by carefully selected and trained pharmacist's mates, of whose performance records the Navy is justly proud. Medical facilities and supplies, although not elaborate, were generally adequate and included sulfonamide drugs and, later, penicillin.

MILITARY SIGNIFICANCE OF HEALTH OF PERSONNEL

Exclusive of those lost on fifty-two overdue submarines, only 62 men died on operations; the causes of death appear in table 1.

The success of a submarine's mission was sometimes compromised by defects in the health of personnel or by defects in the habitability of the ship. Serious or widespread illness was reason for either termination or interruption of approximately 4 per cent of all patrols. The causes of termination of 29 patrols on the basis of illness are listed in table 2.

Personnel fatigue of this magnitude occurred only in the first two years of the war, terminating patrols of eight fleet type submarines. In five other instances, personnel endurance was exhausted and would have

TABLE 1.—*Deaths Occurring Aboard Submarines on War Patrol*

Cause	Number of Men	Number of Patrols
Asphyxiation	26	1
Drowning (lost over the side)	17	13
Battle injuries	12	10
Accidents	3	3
Suicide	1	1
Pneumonia	1	1
Malignant lesion	1	1
Unknown	1	1
Totals	62	31

TABLE 2.—*Conditions of Health Limiting Duration of Submarine Operations*

Condition	Number of Patrols
Excessive personnel fatigue	9
Illness of commanding officer	6
Battle casualties	5
Acute appendicitis	2
Multiple asphyxiations	1
Serious injury	1
Pneumonia	1
Mumps	1
Mental disease	1
Copper sulfate poisoning	1
Unknown (fever)	1
Total	29

terminated the cruise had not operation orders done so. There was nothing unusual about the illness of commanding officers. The remainder of these patrols were terminated consequent to unavoidable hazards and circumstances.

On approximately 2 per cent of all operations, unfavorable habitability became a major factor. On twenty-three patrols, reduced efficiency of operations was caused by or related to impaired habitability. Eight patrols were terminated due to deficiency of environment, the nature of which is listed in table 3.

Ships manned by tired and ill men were not effective fighting units. Illness, when it deprived the submarine of the services of key men, had considerable military significance. The impersonal and abstract qualities of figures make it difficult to convey the immediate importance of these data. However, the actual or threatened impairment of military potentialities which sometimes occurred is apparent in these selected excerpts from war patrol reports:

(On the fourth patrol of the N. [1943]):

Air-conditioning installations proved inadequate. The highest temperature and humidity level recorded was 124 F. (51.1 C.) and 98 per cent, during an invasion period lasting for about thirteen hours. . . . Excessive heat and humidity reduced the efficiency of all hands to a considerable degree after about two weeks of operation.

TABLE 3.—*Factors of Habitability Limiting Duration of Submarine Operations; Military Significance of Submarine Habitability*

Factor	Number of Submarines	Year
Lack of air conditioning	1	1942
Limitation of potable water capacity	4	1942 to 1944
Serious fire (battery)	1	1942
Serious fire (control room)	1	1942
Excessive copper sulfate content of drinking water	1	1944

The P. on her fifth patrol had an experience sometimes encountered in northern operations:

The first dive made . . . lasted longer than expected, with no carbon dioxide absorbent spread. At the end of fourteen hours all hands had difficulty in breathing, carbon dioxide concentration at that time being 2.5 per cent. 800 pounds of oxygen were bled into the boat, bringing slight relief. When the ship surfaced, two hours later, the concentration of carbon dioxide in the conning tower was 3.5 per cent.

The S. was forced to submerge on one occasion on her seventh patrol, an enemy plane having been sighted. While she was still going down, a bomb or depth charge landed on her port side.

A terrific explosion jarred the boat. All hands not holding on to something were knocked from their feet. . . . Fire started in the maneuvering room. All power was lost. . . . Thick, toxic smoke filled the maneuvering and after torpedo rooms. All hands aft were sick. We went up and down three times and had started down the fourth time before power was regained. In the maneuvering room the situation was bad. All hands were violently ill. The angles which the boat had taken had not helped.

(On the second patrol of the P.):

During operations the Commanding Officer collapsed partially and lost the use of his legs, apparently owing to an injury to the spine or the nervous system. This unfortunate illness necessitated return of the submarine to Saipan.

Mass illness cannot help but adversely affect performance aboard a submarine, as aboard the H.:

> Loss of depth control on one attack was most unfortunate in that it prevented firing at a carrier. The order to make ready the tubes had been given rather late. This difficulty was combined with personnel errors in hurriedly preparing all tubes . . . at this time nearly all the crew were handicapped by sickness from food poisoning.

The commanding officer of the S. observed, with regard to illness of personnel:

> Decrease in the number of men in a crew on a long patrol does not permit flexibility of the organization without loss of efficiency when, through illness or accident, a man is placed on the binnacle list.

MEDICAL PROBLEMS

Infections of the Respiratory Tract.—A high incidence of "colds" was commonly experienced within the first three weeks of the cruise, frequently before the submarine reached the operational area. These infections of the upper respiratory tract were sometimes associated with noticeable reduction of personnel efficiency. Patrols in northern operational areas, particularly in the winter, were occasionally handicapped by illness due, in part, to foul weather, the cold and dampness of the interior of the ships, overcrowding and inadequate protective clothing. Colds commonly accompanied the rapid passage from warm to cooler operational areas. The most practical form of prophylaxis was afforded by optimal atmospheric and living conditions while on patrol and by carefully supervised recuperation at rest centers. The effectiveness of germicidal lamps aboard submarines warrants investigation.

Injuries.—The bridge of a submarine offers little protection; men were frequently seriously hurt in heavy weather. Because of the danger of being swept over the side in heavy seas, members of the bridge watch and gun crews and men working topside should be required to wear life jackets, whistles and man lights. The majority of injuries were unavoidable and were incurred while precipitously clearing the bridge or descending through the narrow hatchway. Accidental shifting of skids of torpedo racks in rough seas resulted in two serious head injuries, one of which was fatal. Poorly illuminated hatches accounted for many injuries. In gun attacks approximately 61 men were injured, 12 fatally. Explosions of ammunition seriously injured 8 men.

Diseases of the Gastrointestinal Tract.—Appendicitis caused more anxiety than any other disease; the diagnosis was commonly made by pharmacist's mates. Although the illness interrupted or terminated patrols in 11 instances, not a single death is known to have followed appendicitis originating on a war patrol.

Psychiatric Casualties.—A collection was made of the reports of cases in which disorders could possibly have been neuropsychiatric or emotional in origin. Apparently only those reactions interfering with performance of duty were recorded, for but 56 cases were reported. Statistically, this is an amazingly low incidence of emotional disturbances. In spite of the great responsibilities of commanding officers, there is evidence in the patrol reports of only 4 instances in which a crew lost confidence in their commanding officer or he lost faith in himself. It appears that the "breaking point" was indefinitely deferred and that psychiatric casualties were largely eliminated under conditions which submarines encountered in World War II. The reasons for this are important and have been classified elsewhere [1] in this manner:

1. Initial meticulous selection of personnel.
2. Thorough and specialized training of personnel.
3. High morale, associated wtih success of combat patrols.
4. *Esprit de corps* among submarine crewmen.
5. Adequate facilities for rest and rehabilitation and policies of frequent rotation.
6. Frequent prepatrol and postpatrol medical examinations.

AIR-SEA RESCUE OPERATIONS

Submarines recovered 549 survivors in air-sea rescue operations. The part played by the pharmacist's mates in this undertaking was very important. Forty-eight per cent of the aviators required medical care when recovered from the sea; although 18 per cent were seriously injured, only 2 died aboard submarines.

Submarines assigned to air-sea rescue operations should be especially prepared and equipped to permit increased bunking space and clothing allotments for survivors. Members of the rescue crew must be carefully picked and trained. Pharmacist's mates should be specifically indoctrinated as to the type and treatment of casualties expected.

FACTORS AFFECTING SUBMARINE HABITABILITY

Those conditions most frequently mentioned as influencing habitability were: the inadequacies of ventilation and air conditioning; the discomforts incident to long dives (such as accumulation of carbon dioxide, depletion of oxygen, and increase of pressure and humidity); the weather; overcrowding; deficiencies of the water supply and sanitary tanks; fires; certain noxious agents, such as chlorine gas or carbon tetrachloride, and material damage consequent to depth charging or accidental flooding.

1. Duff, I. F., and Shilling, C. W.; Psychiatric Casualties in Submarine Warfare, Am. J. Psychiat. **8**:607-613 (March) 1947.

Space permits discussion of only the more important components of habitability aboard submarines. In patrol reports, reference was made to habitability as indicated in table 4.

The figures in the table indicate the improvement in habitability which took place as the war progressed: After 1942, the percentage of "excellent" reports was doubled, the percentage of "fair" reports was significantly lowered and the percentage of "poor" reports was cut to one third. Reports of good habitability rose, to remain at a level between 55 and 60 per cent. It may be said, then, that about 70 per cent of all patrols reporting on habitability were made under either good or excellent living conditions.

A relation between reports of poor habitability and success of operations exists, although it is not constant. Thirty-nine of the sixty-three patrols experiencing poor habitability were successful; the majority of those that were not were made in the early years of the war.

TABLE 4.—*Habitability Reports of Fleet Type Submarines*

	1941		1942		1943		1944		1945		Totals	
Rating	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Excellent	0	0	8	8	24	16	41	14	33	16.5	106	14
Good	5	50	34	34	82	55	170	59	117	58.5	408	54
Fair	3	30	33	33	36	24	55	19	44	22.0	171	24
Poor	2	20	25	25	7	5	23	8	6	3.0	63	8
Totals	10		100		149		289		200		748	

Ventilation and Air Conditioning in Relation to Atmospheric Conditions.—Contrary to popular belief, atmospheric conditions within a submarine submerging for a relatively short time are normal. Inasmuch as the hatches are closed before diving, the pressure within the boat is theoretically unchanged; actually, there is a slight rise in pressure, due to such factors as compression of the hull and leaking air tanks. When the ship is surfaced, a current of air is constantly sucked through the main induction valve (located in the superstructure of the ship) to the Diesel engines, and the engines exhaust the air from within the ship, setting up a current of fresh air through the open hatchways. When the ship is submerged, there being no means by which air may be obtained from the outside for combustion, the Diesel engines are shut down. The air contained within the ship is forcibly recirculated after passing through two main and one auxiliary air-conditioning units.

Without adequate air cooling and ventilation, habitability on an active war patrol may become so poor that material defects and decreased personnel endurance may compromise the effectiveness of the ship.

The relation of excess heat and humidity in the conning tower to the efficiency of control parties during long approaches to an enemy target is vital.

To elude antisubmarine activity most submarines at one time or another "ran silent." [2] In only one patrol report was habitability, under such circumstances, reported as "good." Poor atmospheric conditions, the product of excessive heat, humidity, pressure, oxygen depletion and carbon dioxide accumulation, were the rule. The manner in which the extremes of these conditions were tolerated by the carefully selected, trained and disciplined men was extremely important in determining whether a submarine would survive.

With so many sources of heat, the temperature and humidity jumped to high levels in "silent running," particularly in the maneuvering room, where it sometimes reached 125 F. (51.7 C.). All hands stripped down to shorts; socks and shoes were removed, despite which men perspired excessively until, in an hour or so, the decks might be slippery with sweat. Towels used to keep perspiration out of the eyes became wringing wet; shoes and socks could be wrung out like rags. Every one drank a great deal more water than usual and took salt and aspirin tablets. As time went by, the air became oppressive and stifling, and it was difficult to breathe; headaches were prevalent and severe. It was often impossible to sleep; heat rash sometimes caused serious discomfort. The enervation from the heat sometimes became so pronounced that physical exertion, such as that required to change or maintain depth, would exhaust the planesman. Controllermen had to be spelled frequently. Efficiency and reaction times were sometimes reduced considerably; errors were prevalent, even among key men. There was a sharp increase in accidents when the damage of depth charging necessitated long hours of repair work. Constant attention was necessary to see that instructions were carried out properly and promptly. Tempers were short, nerves on edge. The apathy which occasionally developed was startling.

In one extreme case it was reported:

> As the youngsters folded up, the older and more phlegmatic men would take over. Some without permission, others after requesting relief, would quietly leave their stations and lie down on the coolest spots of decking. Occasionally stations ended up with two men taking turns, the off-watch man resting on the deck beside his station. There was no evidence of hysteria, the men carrying out their duties to the limit of physical and mental endurance.

Oftentimes on surfacing there were distressing nausea and vomiting. Under such conditions the ship was no longer in a position to fight or

2. In "silent running," all men except those controlling the ship remained in their bunks; those who had to move about removed their shoes. Talking was kept at a minimum, and all unnecessary noise, including that caused by operation of the ventilation, air-conditioning and refrigeration units, was eliminated.

to defend herself. Though the more severe effects passed off quickly with rest and fresh air, the men were often fatigued and extremely tense for days thereafter.

Ventilation and air conditioning were the subjects for critical comment in over four hundred reports, better than half of which offered suggestions for improvement. Inadequate and unequal distribution of air between the forward and after compartments of the ship and inadequate cooling capacity of the air-conditioning units were the most common complaints. Other frequent criticisms concerned material defects of the air-conditioning apparatus, the hazards of ventilation in heavy weather, and inadequacy of ventilation when submerged. The majority of reports concerning auxiliary ventilation and cooling installations were favorable, although it was sometimes noted that the devices failed to compensate for the basic inadequacies described previously.

Cold and Habitability.—Poor living conditions often prevailed on cold water operations:

> The torpedo rooms were very wet. Metal fittings throughout the ship sweated constantly. Heaters had to be used sparingly to conserve the batteries. With sea water at temperatures of 27 F. (— 2.8 C.), single hull portions of the ship were impossible to heat. There was constantly ice in the torpedo room bilges, and pipes containing water, such as shower drains, were frozen solid.

Excess Carbon Dioxide and Oxygen Depletion.—Limiting values of oxygen and carbon dioxide, after the ship had submerged, were theoretically not attained until the expiration of a period of hours calculated from a formula which, although adjustable, was derived on the basis of peacetime complements and operating conditions. Adequate instruments to measure the amount of carbon dioxide and oxygen were not available. Need for purification of air was commonly based on subjective evidence, such as headache, dyspnea, and failure of the air to sustain a flame. When the need became obvious, varying amounts of carbon dioxide absorbent, which is caustic and irritative, were spread; the atmosphere was further improved by releasing oxygen or compressed air into the ship.

On several patrols, excessive levels of carbon dioxide seriously and adversely affected personnel efficiency. For various reasons, it is difficult to correlate reports of increased levels of this agent with those of associated symptoms. With this in mind and considering the eighty-nine reports containing adequate data, various factors are apparent:

The formula used for calculating the time-limiting values of carbon dioxide and oxygen was not always applicable to wartime operations; the time at which symptoms of intolerance became evident did not necessarily follow the calculated time. In twenty-two of twenty-six reports, the actual period of acceptability of the air ran from one to six hours less than the calculated figure. Half the reports came from

patrols made in northern areas of operations where, because of weather conditions and long hours of daylight, prolonged submerged operations were common. Moreover, the ships were cold and damp, requiring more exertion on the part of each man to keep warm. These factors, in addition to the routine and the increased complement, made it necessary to revitalize the atmosphere frequently.

Purification of air was also a matter of particular concern aboard submarines used as troop transports. On the fifth patrol of the N., when 109 Army Scouts (in addition to the crew of 96) were transported in the Aleutian area, perilous levels of carbon dioxide were experienced, particularly when the Scouts were making ready to disembark. The day preparations were made to land, the level rose to 4 per cent. This defect of habitability, in conjunction with the overcrowding, the cold and the heavy condensation, no doubt explains the statement: "Delay from day to day had a severe effect on most of the Army Scouts . . ."

Much fundamental and careful research has been carried out concerning the physical and mental effects of anoxia and of carbon dioxide poisoning. Studies have been made to improve the available methods of air purification and of detection of undesirable changes in the atmosphere. There was need for positive application of the resultant knowledge to improve submarine habitability; today, with the advent of "schnorchelling,[3]" the need is even greater. The development of an instrument panel in the control room, which would record at all times the oxygen, carbon dioxide, carbon monoxide, hydrogen and hydrocarbon content of the submarine's atmosphere, together with the temperature and the relative humidity, would be a real step forward. It would obviate the necessity of relying on variable subjective symptomatology, inaccurate formulas and obsolete equipment for such fundamental data.

Toxic Gases.—Toxic gases are commonly thought to be a hazard on submarines. It is true that carbon tetrachloride, when used as a cleaning agent, produced distressing and disabling physical effects; for this reason, its use was abolished. Although the formation of chlorine gas, especially after flooding of torpedo battery compartments, was not uncommon, only two serious encounters with it occurred. Formation of arsine and stibine gases in detectable and detrimental quantities was not experienced. Methods for eliminating hydrogen were apparently satisfactory. Thus, the problem of toxic gases aboard submarines is seen to have been more potential than actual in World War II. Of much greater significance were the relatively simple factors of extreme heat and humidity.

3. "Schnorchelling" is the obtaining of air for the Diesel engines from above the surface of the water when the submarine is submerged.

Fires.—The relation between fires and habitability was important. The dense, black clouds of smoke quickly spread throughout the compartments. The acrid, phenolic fumes were not only irritating and blinding but also extremely nauseating. With the intense heat, compartments quickly became untenable. The toxic, blinding and demoralizing effect of smoke emphasizes the necessity for thorough and frequent instruction in the operation of protective equipment, without which men may be quickly overcome. Adequate and effective firefighting equipment is a necessity.

Potable Water Supply.—In the early days of the war, limitation of fresh water was cause for great concern and was a factor limiting the duration of a few patrols. Fortunately, evaporating units of today are reliable in service and are capable of producing an entirely adequate supply of fresh water.

Condensate from the air-conditioning apparatus was used to augment the supply of fresh water. Dr. George Schiff made a war patrol aboard a submarine to study the problem and concluded that by filtration sufficient condensate could be chemically and bacteriologically purified to make 300 gallons available for daily general use. Condensate was utilized for bathing, in washing machines and for general cleaning. Various methods of collection and storage were in use. In view of the critical nature of weight and space aboard submarines there were no authorized provisions for storage beyond installation of a 20 gallon tank for collection of condensate to be used in washing machines.

Impairment of potability of fresh water sometimes occurred. On a number of patrols, contamination with copper sulfate took place at levels sufficient to impair efficiency of personnel; it was the cause of termination of one patrol. It appears reasonably certain (from investigations carried out at the Naval Medical Research Institute) that copper and nickel were derived from the action of vapor and hot water on the metal tubes in the stills. Future arrangements call for their replacement by tubes coated with tin. When this is done, contamination of water with copper sulfate may be important only historically.

Submarine Ration.—The inherent limitations and discomforts of life aboard submarines made imperative special efforts to provide a good ration. Food was excellent and deserved the reputation which it came to have among other less elaborately fed branches of the service. Certain problems existed, however. More active participation by squadron medical officers is needed to assure submarines of a satisfactory ration. The whole problem should be investigated with a view toward constructing an exact, although flexible, master ration plan. More thorough schooling of commissary officers, stewards, cooks, bakers and

supply officers is indicated. The two dietary factors most commonly the cause for complaint were the quality and amount of boned beef. Submarines should be given a high priority, especially at advanced bases, to obtain frozen fruits and vegetables, whose importance was amply demonstrated. Certain luxury foods are important to provide variety and to enliven what otherwise may be a monotonous diet. The significance and importance of ice cream in providing variety in the diet and as a morale builder are apparent [4] from patrol reports.

Sanitary Tank Head System.—Waste products from the lavatories and galley were collected in sanitary tanks. Military security prevented emptying of the tanks except on surfacing under cover of darkness; the tanks were then blown dry with compressed air. They could be flushed with sea water only with difficulty. On a long patrol, despite frequent emptying and the use of various disinfectants, the tanks became unpleasantly odorous and were the cause for many justified complaints. Correction of this essentially mechanical defect should not be too difficult. One may conjecture, in this respect, to what extent the present problem might become magnified aboard submarines equipped for schnorchelling and submerged for long periods.

Overcrowding.—Bunking facilities aboard many submarines were designed for peacetime complements, which were increased as the war progressed. With the addition of electronic apparatus and new types of torpedoes which required frequent routining, the shortage of space became more and more critical. Adequate provision for bunking and personal needs could not be made. Overcrowding on the average patrol probably produced no lasting effect on personnel efficiency. On submarines used in air-sea rescue operations and as troop transports, serious overcrowding was experienced. In preparing for the future, the use of submarines for such purposes merits review in the light of lessons so recently learned.

Protective Clothing.—To maintain a reasonably long and alert watch in the most severe weather, bridge personnel must remain comfortably warm and dry. Adequate protection of the face, hands and feet is fundamental. On cold water operations it was apparent that the available items of protective clothing were woefully inadequate. Production of improved garments, with the special needs of the submarine service in mind, should be investigated. Designs of clothing must be practical and tailoring neat, with a minimum of bulk, to facilitate rapid and easy clearance of the bridge and easy stowage. Material must incor-

4. Shilling, C. W., and Duff, I. F.: Analysis of Submarine Food Problems in World War II, U. S. Nav. M. Bull. **48**:683-697 (Sept.-Oct.) 1948.

porate a minimum of weight and bulk and a maximum of durability, practicability and safety; it should have rapid drying qualities. Great merit exists in the recommendation for a satisfactory one piece exposure suit.

OTHER FACTORS INFLUENCING PERSONNEL ENDURANCE

Length of Operations.—In 1941 and 1942, little was known concerning the length of war patrols which men might be expected to tolerate. Accumulated experience tended to modify some of the earlier impressions.

At the time of leaving the area of concentrated activities, an attempt was made by the commanding officer to estimate the remaining days of personnel endurance. The figure was arrived at subjectively. Though it was reported as "0" days on twenty-five patrols, such an evaluation did not necessarily mean that the crew was in a state of collapse, but rather that the men were no longer on their toes and that their fighting efficiency had dropped. Early evidence of fatigue was commonly observed about the fortieth to the fiftieth day on station.

A patrol carried out in good weather with plenty of targets, good fire control and freedom from depth charges could last far longer than one on which any of these features was missing. The monotony of a submerged patrol without contacts was extremely fatiguing unless some diversion or change of pace was introduced. Short, aggressive patrols were said to take as much or more out of the men than did the longer patrols. If lulls in activity occurred, material reduction in efficiency could be forestalled. If not, fatigue began to be apparent. Although aggressiveness and desire to close with the enemy may not have slackened, the fighting edge of the ship was definitely impaired in that the reserve strength of the crew to meet possible emergencies was lacking. Failure to "shift to the second string" under such circumstances was sometimes cause for regret. On such occasions fatigue might become dangerous, the condition of the crew approaching physical and nervous exhaustion. The last week of patrol was generally the hardest. Recuperation during the quiet return voyage was oftentimes noticeable and sometimes acted to create a false impression of the crew's endurance on arrival at port. When fatigue was excessive, recuperation might not take place, especially when considerable action had been experienced in the last week on station.

Extensive surface operations, while inherently decreasing the amount of rest, increased the general well-being of the crew. On prolonged submerged operations, a routine was necessary which kept efficiency at the highest level. Continual rough seas, with "colds," seasickness, need for securing air from the outside and inability to sleep

produced a most depressing effect. Under such circumstances, withdrawing from station for a short rest was authorized.

The question of how long men might efficiently make consecutive patrols was the subject of much interest. There is no all inclusive answer. Some men made an astounding number of war patrols without apparent ill effect. The receipt of "new blood," through the enforced rotation policy, resulted in general improvement in spirit and workmanship, which was conducive to an aggressive spirit and to a closely integrated crew.

Morale.—A high state of interest and aggressive determination was essential to the success of operating submarines and was closely related to personnel endurance and morale. The greatest single factor contributing to a high state of morale was successful engagement with the enemy. Once a new ship had successfully completed a patrol, the battle had been half won. All hands then felt their footing to be secure, for they had ceased to be a "detail" and were, instead, a fighting unit. There was nothing so shocking as a "zero run," especially to the crew of a ship with a long record of success. On patrols characterized by disappointment, lost opportunities and lack of worth while contacts, poor performance of the deck watch might be observed. As the war progressed and targets became less common, the "lethargy of long diving days, of rough sleepless nights and limited exercise had to be mitigated by a clear portrayal of the part submariners were playing in the over-all strategic and tactical plans." The highest qualities of leadership on the part of the officers and alert patience on the part of all hands were essential.

There were many "creature comforts" which were vital in maintaining morale. These included good food, mail, movies, books, magazines, phonograph and rebroadcast records, adequate quantities of fresh water, mascots, church services, favorable publicity and the possibility of "new construction," with the attendant four to six month period of "States-side" duty. The great importance of adequate and comfortable facilities to permit rest and recuperation at the end of patrols contributed greatly, with the foregoing factors, to the sustained pattern of success which characterized submarine warfare in World War II.

MEDICAL CARE AND FACILITIES AVAILABLE TO SUBMARINES

The advantages of having specially trained medical observers aboard operating submarines for research purposes are obvious, as is the desirability of having a physician attached to one of a group of submarines on air-sea rescue operations. Medical officers especially experienced in submarine medicine are needed at advanced bases, where

they should be attached to submarine squadrons. They should familiarize themselves with the ships and develop a close liaison with commanding officers and pharmacist's mates. Certain medical conditions (unusual fatigue, chronic recurrent appendicitis, chronic seasickness, inability to equalize for increased pressure, active venereal disease, tuberculosis) should be detected and corrected, for they not only may be disqualifying but may interfere with personnel efficiency. Men showing evidence of emotional tension must be carefully evaluated before being permitted to return to submarines. Transfer at sea of injured and ill personnel was frequently necessary, and facilities to accomplish this rapidly and safely under the most adverse conditions must be available.

SUMMARY

The reports of fourteen hundred and seventy-one submarine war patrols made during World War II have been studied to evaluate the human factor in problems of submarine combat.

No health problems entirely peculiar to the submarine service exist. As in all other branches of the military forces, the commonest causes of man-days lost aboard submarines on combat patrol were acute infections of the upper respiratory tract, injuries, and diseases of the gastrointestinal system. That not a single death occurred from appendicitis originating on a war patrol is attributable to intelligent medical care by well trained pharmacist's mates.

In the nearly four years of the war, only 62 deaths from all causes (including battle injuries) occurred aboard submarines on patrol, exclusive of those lost on overdue ships. While the health of submarine personnel was generally excellent, it is significant that serious individual or mass illness terminated or interrupted twenty-nine of fourteen hundred and seventy-one patrols.

Despite the special hazards under which submarine crews lived and fought, which are popularly thought to contribute to psychiatric breakdown, the actual psychiatric casualty rate, as shown in the reports, was amazingly low. This record is essentially a reflection of careful selection of personnel.

The medical problems peculiar to submarines arise from unfavorable changes in habitability, which occur chiefly in combat. The most important of these are excess heat and humidity, the accumulation of carbon dioxide and the depletion of oxygen from the air. That only thirty-one patrols in World War II were interrupted or terminated because of these or other deficiencies of habitability speaks well for the progress which was made in control of these problems. Until these deficiencies have been completely overcome, they will continue to be a limiting factor in submarine operations.

TRAUMATIC CORONARY THROMBOSIS WITH MYOCARDIAL INFARCTION

Postmortem Study

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IN THE rapidly expanding literature on nonpenetrating injury to the human heart, there is scant reference to direct damage to the coronary arteries by such blunt injury. A rare case of this type, with detailed clinical and postmortem studies, is reported at some length, as it appears to be an authenticated instance of thrombosis of the coronary artery with consequent myocardial infarction, produced by a contusion of the anterior wall of the chest.

REPORT OF A CASE

C. B., a woman, was first admitted to the Mount Sinai Hospital in November 1945, when she was 49 years of age. Renal disease of unspecified type developed at the age of 31, during her second pregnancy. At the age of 37, a laparotomy was performed with the removal of a pelvic tumor; postoperative radiation treatment was given. Early in 1945, hypertension was first brought to her attention. The systolic reading was then 200 mm. of mercury. Three days prior to her first admission to the hospital in November 1945 she felt faint, and, on attempting to leave her bed, she collapsed, striking the left side of her face and sustaining multiple bruises. Dizziness and severe headache persisted for the next three days, and she was admitted to the hospital. She was pale and lethargic. The fundi oculorum presented moderately severe vascular changes, with gray nerve heads and diffuse flat edema obscuring the margins of the disks; the arterioles were narrowed. Numerous exudates and hemorrhages were scattered throughout the retinas. The lungs were clear on auscultation. The apical impulse was forceful and was felt in the fifth interspace. The heart sounds were of good quality. A systolic murmur was heard at the apex. The basic second sounds were of equal intensity. The blood pressure was 240 systolic and 115 diastolic. The electrocardiogram (fig. 1) showed regular sinus rhythm, a diphasic T wave in lead I and a shallow T wave in lead II. Roentgenographic examination of the chest revealed slight enlargement of the left ventricle. The circulation time, arm vein to tongue, by the calcium gluconate method, was 14 seconds. The circulation time from arm vein to lung by the ether method was 7 seconds. Both readings were within normal limits for these methods. The venous pressure was normal, measuring 75 mm. of water. Lumbar puncture was readily performed and showed fresh blood, evidence of recent subarachnoid bleeding. Treatment consisted of sedation, the use of the Kempner rice diet, magnesium sulfate by mouth and hypertonic glucose solution intravenously. On this regimen, the blood pressure slowly dropped

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and the headache remitted. The patient was discharged from the hospital on the twenty-seventh day, having weakness and asynergy of the left upper extremity as the residua of the cerebrovascular insult she had undergone shortly before her admission.

During the ensuing eight months, she remained in relatively good health, complaining only of some weakness of the affected extremity and slight dyspnea on exertion. On Sept. 10, 1946, she was driven by her son into the country. The driver lost control of the automobile, which crashed into a telephone pole. The patient, seated in the rear of the car, was thrown forcibly forward against the back of the front seat, resulting in a contusion of the anterior wall of the chest. There was no loss of consciousness. Her first recollection was of squeezing pain in the left side of the chest and of some difficulty in catching her breath. She later

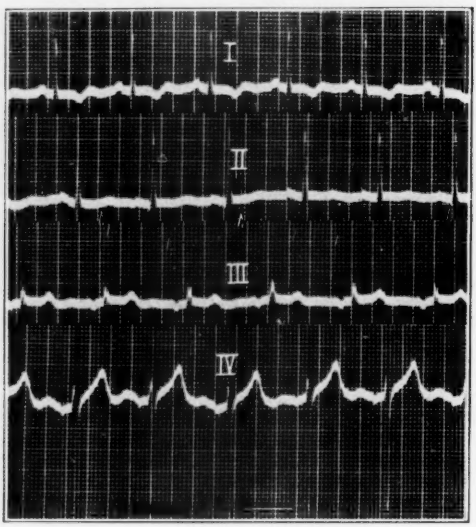

Fig. 1.—Electrocardiogram taken Nov. 8, 1945 during patient's first admission to the hospital. The changes in the T wave are those commonly seen in hypertension.

described the sensation as a feeling that "two bones were being squeezed together." After preliminary roentgenographic examinations at a nearby hospital proved negative for skull fracture, she was brought to the Mount Sinai Hospital, eight hours after the accident. On examination much bruising was in evidence, especially about the left midchest and the left orbital area. The pupils were round and regular and reacted to light and in accommodation. The right fundus was visualized and showed narrowed, tortuous arterioles. The margins of the disk were clear. A few small hemorrhages were seen. A large ecchymosis, of the size of a football, occupied the left anterior wall of the chest, close to the sternum (fig. 2). The apical impulse was again felt in the fifth interspace, slightly to the left of the midclavicular line. Gallop rhythm was present. A systolic murmur was

heard at the apex. Minor lacerations, bruises and ecchymoses were distributed over the extremities.

The first electrocardiogram (fig. 3) was taken on the day following the patient's admission to the hospital. It showed sinus tachycardia and the rate of 105 beats per minute, with a small Q wave in lead I and a deep Q wave in lead IV. The RS-T segments in leads I and IV were elevated. The RS-T segment in lead III was depressed. The T waves in leads I and IV were depressed. These changes are typical of acute coronary thrombosis with myocardial infarction of the anterior wall of the left ventricle.

On this same day, the white blood cells numbered 10,900, with 83 per cent polymorphonuclear forms. Other laboratory findings included a bleeding time of 3 minutes. The clotting time was 7½ minutes (Lee-White method). The prothrombin index was 100 per cent, the control and prothrombin time both being 16 seconds. The icteric index was 3. The ascorbic acid level of the blood was 7.8 gamma per cubic centimeter of serum. The reaction to the tourniquet test was weakly positive. The thrombocyte count was 210,000 per cubic millimeter.

Fig. 2.—Photograph of patient, in bed, one week after accident, showing large ecchymosis of anterior wall of the chest.

The sedimentation rate of the red blood cells on the third day after admission was 39 mm. per hour (Westergren method). The blood urea nitrogen was 14 mg., blood sugar 85 mg., total cholesterol 435 mg. and total serum protein 8 mg. per hundred cubic centimeters. The specific gravity of the urine ranged from 1.018 to 1.022. The urine gave a 1 plus reaction for albumin; there was no glycosuria. The pain experienced immediately after the accident persisted in variable degree for two days, and on the third day the patient was free from pain in the chest. Gallop rhythm was still present, however. She lay quietly in bed, neither dyspneic nor orthopneic. The temperature remained elevated for the first six days, slowly dropped to normal in the next two days and remained normal for the last four days.

Another electrocardiogram (fig. 4), taken on the tenth day after admission, showed the return of the R-T segment to the isoelectric line in lead I, with inversion of the T wave; a deep Q wave and some elevation of the R-T segment remained in lead IV. Routine hospital rounds on the morning of the thirteenth day found the patient comfortable. The lungs were clear on auscultation; the cardiac rhythm was regular. The heart sounds were of good quality and the

gallop was no longer heard. The cardiac rate was 88 beats per minute. Three hours later, at noon, she was observed by the nurse to be in a convulsive seizure. There were generalized tonic convulsions and apnea. Artificial respiration, as well as intracardiac drug therapy, was of no avail in restoring cardiac function. The heart sounds and pulse were unobtainable prior to the failure of respiration.

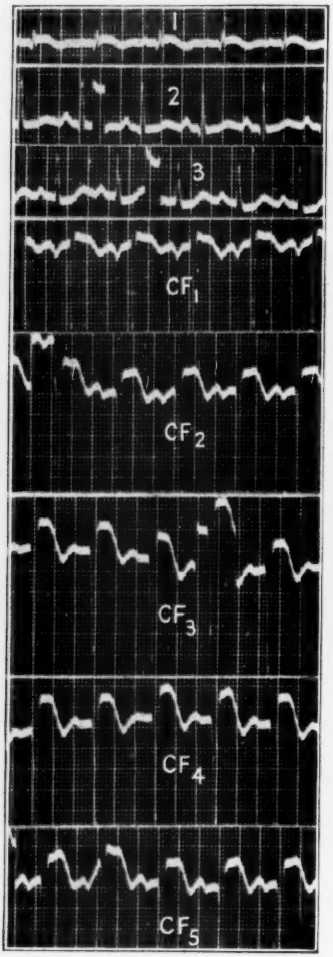

Fig. 3.—Electrocardiogram taken on the day after accident. Q waves are seen in lead I and the precordial leads, with elevated R-T transitions, on the basis of which diagnosis of coronary thrombosis with infarction was made.

Autopsy was performed five hours after death. Numerous areas of ecchymosis were evident over various parts of the body, especially about the orbits. On the anterior wall of the chest, in the precordial area, a large, irregular ecchymosis, measuring 6 by 8 cm., was visible. No costal fracture could be made out. The right pleural cavity contained 300 cc. of clear straw-colored fluid; 200 cc. of a similar fluid was obtained from the left pleural cavity. The right lung was adherent to the fourth, fifth and sixth ribs laterally by firm fibrous bands. The remainder of the pleural surface was smooth. The pericardial surfaces were smooth and glistening. A small quantity of pericardial fluid, blood stained and about normal in amount, was present. The heart weighed 410 Gm. Several needle punctures were seen, the evidence of intracardiac therapy. No ecchymoses were apparent on

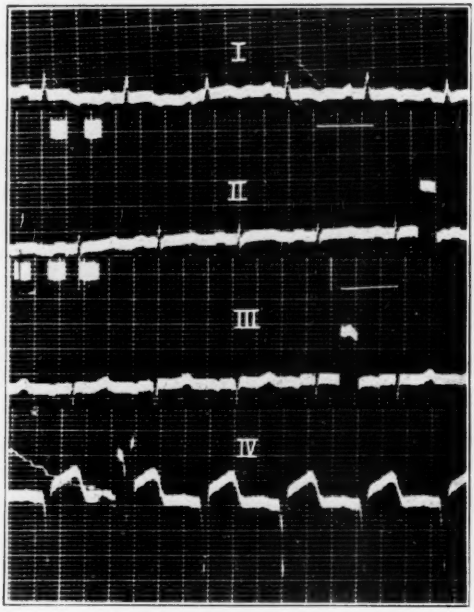

Fig. 4.—Electrocardiogram taken on the tenth day after the accident, showing progressive changes of myocardial infarction.

the surface of the heart. A large myocardial infarct was present and comprised the anterior half of the interventricular septum, the lower half of the anterior wall and the entire apex. These areas showed widespread confluent necrosis surrounded by red zones. Within the infarcted area on the anterior apical surface there was a depressed, irregular, dark red, mottled zone, measuring 5 by 4 cm. Two similar areas, 1.5 cm. in size, were present on the posterior surface of the apex, on either side of the septum. The myocardium and the endocardium of the auricles were not noteworthy.

The right ventricular wall measured 3 to 4 mm. posteriorly. The lower portion of the septum showed yellow discoloration of the trabeculae. Within the

anterior cusp of the tricuspid valve was a 5 mm. hemorrhage. The tricuspid ring measured 9.5 cm. The pulmonary valve was not remarkable; its ring measured 6.5 cm. The mitral valve was essentially normal, its ring measuring 7.5 cm. The left ventricular wall was unusually thick and firm, measuring 2 cm. On horizontal section through the anterior wall and septum, the necrosis was seen extending up to a level of 4 cm. from the origin of the left main coronary artery. Higher sections showed that the reddish depressed areas of repair extended up to a level

Fig. 5.—Photomicrograph of transverse section of the descending branch of the left coronary artery at site of thrombosis, showing the large subintimal hemorrhage; × 7.9.

2 cm. from the orifice, where they involved the myocardium without reaching the subpericardial fat tissue.

The left anterior descending artery was occluded completely by red and gray adherent material, beginning 3 cm. from the orifice and extending for a distance of 1 cm. On cross section, the lumen was occluded mainly by a dark red material.

On one side this material was completely separated from the wall of the vessel by a thin, circular, gray layer. Between this zone and the vessel wall a yellowish white substance was present. Proximal and distal to the site of occlusion the artery showed advanced sclerosis and calcification with narrowing. The left circumflex and the right coronary arteries were about one-half the size of the left coronary artery. The aorta presented pronounced intimal sclerosis and thickening with elevated yellowish white patches.

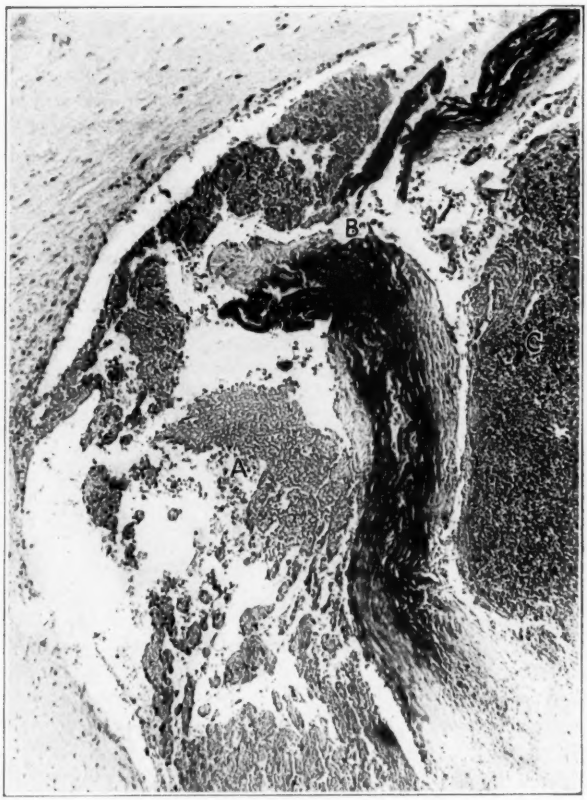

Fig. 6.—High power magnification of blocked-off area in figure 5, showing thrombus (*A*); rupture of intimal lining (*B*), and subintimal hemorrhage (*C*); × 74.

The lungs showed no evidences of laceration. There were firm fibrous adhesions of both lungs, obliterating the interlobar fissures. The basal portion of the lower lobe of the left lung and the entire lower lobe and the middle lobe of the right lung were purple, fleshy and airless. Thre was considerable oozing of frothy blood

from the freshly cut sections of the lung. The pulmonary vessels appeared normal. Other observations included hydronephrotic contraction of the left kidney, secondary to intrinsic constriction of the left ureter by old scar tissue; stenosis of the recto-sigmoid portion of the intestine due to the same cause; amyloidosis of the glomeruli and of the arterioles of the heart, liver, spleen, pancreas, kidney and adrenal glands.

Finally, the brain showed severe arteriosclerosis of the vessels of the cerebrum, cerebellum and spinal cord, with encephalomalacia and scarring in the cerebellum. In the left cerebellar hemisphere at the point where the middle cerebellar peduncle meets the white matter of that hemisphere, a triangular defect was observed, measuring about 6 cm. Its lining was yellowish, and it was surrounded by a narrow zone of yellowish tissue. This yellow zone could be traced into the lateral wall and roof of the fourth ventricle. This was an old area of softening with hemorrhage and extravasation of blood into the ventricular system. The blood vessels in this affected area showed prominent changes—hyalinization of the vessel walls and occlusion of many small vessels and capillaries. The walls of the larger vessels were thickened, and thrombus formation was evident. The changes in the blood vessels of the cerebral cortex and of the spinal cord were similar, although less extensive.

Microscopic examination of a section of the left ventricle revealed early acute myomalacia, with large islands of muscle showing loss of striation and of nuclei and surrounded by fibroblastic and capillary proliferation. Section of the interventricular septum showed acute myomalacia, with replacement of necrotic muscle fibers by loose fibrous tissue, capillaries and infiltration of round cells. The left anterior descending branch of the left main coronary artery was decidedly atherosclerotic, and there was a hemorrhage into an atherosclerotic plaque (fig. 5). The extremely narrowed lumen was occluded by a recent thrombus (fig. 6). Both the myocardial infarct and the occluding thrombus were of a histologic age consistent with the time elapsed from the day of the accident to the day of death, namely, thirteen days.

COMMENT

It is now generally accepted that nonpenetrating blows to the chest can cause myocardial damage. There is ample evidence, both experimental and clinical, to support this view. The experimental investigations of Schlomka [1] demonstrated that lesions of the cardiac muscle can be produced by blows delivered to the chest of animals. Using cats and rabbits for the most part, Schlomka struck blows of moderate severity to the unexposed wall of the chest. In some animals, he observed localized myocardial hemorrhage and, more rarely, tears into the wall of the heart muscle. He was of the opinion that localized blows transmitted to the precordium induced spasm of the coronary arteries in much the same manner that gunshot wounds of the extremities cause traumatic segmental arterial spasm when penetration of the tissue is close to the artery. To this spasm of the coronary arteries and the resulting myocardial ischemia, Schlomka ascribed the functional and anatomic alterations noted. Functional changes included various types of arrhythmia, heart block and electrocardiographic abnormalities, many of which were transient.

1. Schlomka, I.: Commotio cordis und ihre Folgen, Ergebn. d. inn. Med. u. Kinderh. **47**:1, 1934.

In the experimental study of Kissane, Fidler and Koons,[2] blows were delivered to the unexposed chests of anesthetized dogs. The cardiac lesions produced were chiefly subendocardial and pericardial hemorrhages. These hemorrhages varied from small petechia-like spots to large areas of bruising and discoloration. The myocardial hemorrhages and contusions were also seen to extend into the muscle wall from the local areas of bruising on the pericardium and the subendocardium. In some of the dogs, pericardial tears were observed. The authors postulated edema of the heart muscle to account for the sudden and transient electrocardiographic changes seen in several of the animals in which no cardiac lesions were observed at autopsy.

From clinical studies of nonpenetrating trauma to the chest one can draw on cases which illustrate the wide range of cardiac injuries, from the mildest contusion, with minimal signs and symptoms which are often overlooked, to rapidly fatal rupture with cardiac tamponade. In 1935, Bright and Beck [3] collected from the literature all the cases of nonpenetrating cardiac injuries and grouped them under three headings. In the first group, numbering 12 cases, the accident was survived but cardiac failure and irregularities in rhythm were exhibited. The second group comprised 11 cases in which death was due to cardiac failure. The third group included 152 cases of cardiac rupture, all established by necropsy.

Cardiac rupture may occur during the second week after injury, at the time of greatest softening of the contused muscle. Such was the sequence of events in the case reported by Tuohy and Berdez.[4] A 63 year old man was injured in a steering wheel accident. He continued to be ambulatory, although he complained of faintness and vomited daily. Two weeks after the accident, while he was in a motion picture theater, he collapsed immediately after a hearty laugh and was taken from the theater dead. Autopsy revealed rupture of the left ventricle near the apex.

Equally dramatic is the story of the 9 year old boy whose chest was pressed against a wall by a cart.[5] Examination soon after the accident failed to show evidences of external injuries. There were no fractured ribs. As the boy felt quite well on the following day, he was permitted to return to school, where he engaged in the usual games without discomfort. During the next ten days he made no complaints, but on

2. Kissane, R. W.; Fidler, R. S., and Koons, R. A.: Electrocardiographic Changes Following External Chest Injuries to Dogs, Ann. Int. Med. **11**:907, 1937.

3. Bright, E. F., and Beck, C. S.: Nonpenetrating Wounds of the Heart, Am. Heart J. **10**:293, 1935.

4. Tuohy, E. L., and Berdez, G.: Two Instances of Perforation of the Heart Following Non-Penetrating Chest Injury, Minnesota Med. **9**:144, 1926.

5. Gunewardene, H. O.: Traumatic Rupture of Heart Without External Injuries, Brit. M. J. **2**:942, 1934.

the eleventh day after the injury while playing at school, he experienced precordial pain, collapsed and died. At postmortem examination, hematopericardium and rupture of the anterior surface of the left ventricle were observed.

The mechanism of cardiac damage in such cases is clear. The force of the external violence is transmitted to the heart muscle, which undergoes varying degrees of reaction depending on the intensity of the impact. In milder injuries, small contused areas with focal hemorrhage may be the only pathologic change, giving rise to few, if any, symptoms. At times, transient arrhythmias and evanescent electrocardiographic changes occur. The most violent blows cause such disruption of muscle fibers as to lead to either immediate or delayed rupture. Between these extremes are many recorded cases of myocardial damage with areas of thinning and aneurysmal dilatation of the ventricular wall, death occurring at some time remote from the accident. While the sequence of events in these remote cases might be open to question in some instances, there are on record illustrations such as the following ones, in which the pathologic changes unquestionably are related to the injury.

A boy 12 years of age was run over by a wagon and had multiple fractures of the ribs on the left side.[6] Except for occasional attacks of palpitation and vomiting, he remained in good health to the age of 24, when paroxysmal auricular flutter set in; during these attacks, heart failure developed. He died suddenly at the age of 25. Autopsy disclosed a large aneurysm at the apex of the left ventricle. The anterior descending branch of the left coronary artery was interrupted at the upper limit of the aneurysm. One can only surmise whether the artery was damaged directly by the blow, leading to thrombosis of the artery with cardiac infarction and aneurysm, or whether both the artery and the adjacent muscle wall were destroyed by the trauma. There seems little doubt of the relation of the trauma to the observations at autopsy in this young man.

Direct trauma to the coronary arteries with the formation of coronary thrombosis and secondary myocardial infarction has been repeatedly considered a probable mechanism in cardiac trauma. A priori, there is no reason that these vessels, lying superficially on the muscle wall, should not be subject to direct damage, particularly when diseased and brittle. But to date, records of such an accident in which the observations are beyond question are few. However, several reports of lesions seen at autopsy strongly suggest this mechanism of muscle damage.

6. Joachim, H., and Mays, A. T.: A Case of Cardiac Aneurysm Probably of Traumatic Origin, Am. Heart J. **2**:682, 1927.

Schminke [7] reported the history of a 45 year old man who was struck by a wagon shaft. After a short period of unconsciousness, he complained of severe pain in the chest and left arm. For the next six months he continued to experience pain in the chest provoked by climbing stairs and other forms of activity. He died suddenly six months after the accident. Autopsy revealed organized thrombi in the anterior descending branch of the left coronary artery and in the circumflex branch of the right coronary artery. Extensive myocardial scarring with an aneurysm at the apex of the left ventricle was evident.

Damage to the coronary arteries is referred to in Warburg's monograph.[8] One reference is the case just cited. In a subsequent report dealing with the same subject,[9] Warburg mentioned other cases which came to his attention. One was reported by Fraenkel in 1917.[10] A 20 year old soldier died in cardiac failure six months after being injured in a shell explosion. At autopsy, an aneurysm of the left ventricle was observed. The descending branch of the left coronary artery showed aneurysmal dilatation and was blocked by a thrombus.

Warburg [9] further detailed a personal communication from Muller concerning a man aged 59, who was struck by a bicycle and fell on his chest and abdomen. He subsequently complained of substernal oppression which appeared when he walked upgrade or climbed stairs. On the ninth day after the accident, he had a severe nocturnal attack of angina pectoris; this was followed by fever, leukocytosis and typical changes in the R-T segment in the electrocardiogram which justified the diagnosis of coronary thrombosis. Two weeks after the accident, the patient died in cardiac failure. Necropsy revealed thrombotic occlusion of the descending branch of the left coronary artery with a large infarct and recent pericarditis. There was arteriosclerosis of the occluded branch, and to a lesser degree of the other branches. Further details were not given. It must be assumed that the examiner considered the age of the thrombus and the infarct to correspond with the date of injury. If so, the case history is similar to the one being reported.

Randerath [11] cited the history of a 34 year old soccer player who was struck in the chest by a ball kicked from a distance of 5 meters. He

7. Schminke, A.: Beitrag zur traumatischen Aetiologie der Arteriosklerose, Deutsches Arch. f. klin. Med. **149**:145, 1925.

8. Warburg, E.: Subacute and Chronic Pericardial and Myocardial Lesions Due to Non-Penetrating Traumatic Injuries: A Clinical Study, New York, Oxford University Press, 1938.

9. Warburg, E.: Myocardial and Pericardial Lesions Due to Non-Penetrating Injury, Brit. Heart J. **2**:271, 1940.

10. Fraenkel: Herz mit thrombosiertem Aneurysma der linken Kranzarterie, Deutsche med. Wchnschr. **43**:159, 1917.

11. Randerath, E.: Frühveränderungen des Herzens nach Commotio Cordis, Verhandl. d. deutsch. path. Gesellsch. **30**:163, 1937.

immediately collapsed, with pallor and cold sweat. The pulse was small and quick. There was tenderness to the left of the sternum on palpation. On the following day, after a temporary improvement in the circulation, there was recurrent collapse and, at the same time, sudden coldness and pallor of the right lower extremity. The patient died on the second day after the blow to the chest. No electrocardiograms were taken.

Pertinent necropsy observations included slight ecchymosis to the left of the sternum in the region of the fifth and sixth ribs. There was no pericardial effusion; the pericardium was normal. The heart weighed 370 Gm. and was soft, particularly at the left ventricular wall. At the apex a small flat recent aneurysm of the left ventricle with fresh mural thrombi was seen. An embolus was described as being lodged in the proximal portion of the descending branch of the left coronary artery. Another embolus was observed at the proximal end of the right coronary artery. Early arteriosclerosis of the coronary arteries was evident. The severest necrosis was located in the wall of the left ventricle. The anterior papillary muscle was ruptured.

Thrombus material was lodged in the right femoral artery. The occlusive lesions of both the coronary arteries and the femoral artery were considered embolic in origin, arising from the mural thrombi within the cavity of the left ventricle. This case is unusual in many respects, particularly in the formation of an early aneurysm of the ventricular wall and the development of emboli, all within two days. Macroscopically, the aneurysm at the apex and the gray color of the endocardium suggested a less acute process than indicated by the history. Microscopically, however, the process appeared to be acute, displaying normal interstitial tissue in areas of extensive necrosis of muscle fibers.

Of 3 cases of traumatic coronary infarction found in a study of 9,629 consecutive postmortem protocols,[12] Bean described briefly the history of a man who fell 8 feet (2.4 meters) from a ladder and struck his chest, fracturing several ribs on the left side. Severe pain was experienced for a day. Death occurred ten weeks after the fall, and at autopsy a fairly recent infarct with early aneurysmal dilatation was observed. The other 2 cases are presumptive examples of traumatic infarction.

A study of such autopsied material gives some insight into the probable frequency of myocardial damage of varying degree due to external violence. There are also many recorded instances in which recovery took place, but in which the injury was followed by classic signs, symptoms and laboratory evidence of acute myocardial infarction.

12. Bean, W. B.: Infarction of the Heart: A Morphological and Clinical Appraisal of Three Hundred Cases; I. Predisposing and Precipitating Conditions, Am. Heart J. **14**:684, 1937.

The case of the accident with a golf ball has been cited and recited and is now legend.[13] A 57 year old man was struck in the chest by a golf ball. He was temporarily shocked but returned to work for the next two days. Attacks of angina pectoris occurred on the third day, and an electrocardiogram showed evidence of fresh myocardial infarction.

Equally convincing are the cases reported by Kienle,[14] Boas,[15] Sigler [16] and Hecht.[17] One cannot deny that each of these reports gives reasonable proof of the presence of myocardial infarction following trauma. The immediate development of pain, coupled with disability, fever and electrocardiographic changes, provides fairly indisputable evidence of myocardial infarction with necrosis of muscle. But from the clinical history alone one cannot determine the underlying mechanism of the infarction. It may be due to coronary thrombosis or to prolonged coronary spasm without obstruction of the lumen, such as is implied in experimental work,[1] or, finally, to severe contusion of the muscle itself without involvement of the coronary arteries either by spasm or by occlusion.

Friedberg and Horn [18] observed myocardial infarction without recent coronary thrombosis in 31 per cent of a group of 34 nontraumatic cases, taken from a total of 2,000 autopsies. They ascribed the myocardial damage to intense coronary insufficiency, precipitated by abnormally increased demands on the coronary circulation, already compromised by narrowing. Moritz and Atkins [19] likewise observed that in 20 human cases with large cicatrized infarcts, the site of remote coronary occlusion could be identified in only 9 instances. This is not remarkable in the light of the observations of Friedberg and Horn, and in view of the now generally accepted role of coronary insufficiency due to shock, loss of blood and unusual physical demands on the coronary circulation, in the production of acute muscle necrosis. Indeed, in cases of trauma among persons of the older age groups in which shock is a prominent

13. Relation of Myocarditis and Coronary Thrombosis to Trauma, Queries and Minor Notes, J. A. M. A. **101**:1503 (Nov. 4) 1933.

14. Kienle, F.: Klinische und elektrokardiographische Beobachtungen bei traumatischem Hinterwandinfarkt, Ztschr. f. Kreislaufforsch. **30**:674, 1938.

15. Boas, E. P.: Angina Pectoris and Cardiac Infarction from Trauma or Unusual Effort, J. A. M. A. **112**:1887 (May 13) 1939; Some Immediate Causes of Cardiac Infarction, Am. Heart J. **23**:1, 1942.

16. Sigler, L. H.: Trauma of the Heart Due to Nonpenetrating Chest Injuries, J. A. M. A. **119**:855 (July 11) 1942.

17. Hecht, H. H.: Heart Trauma: Myocardial Involvement (Contusion) Following a Non-Penetrating Injury to the Chest (Airplane Accident), Ann. Int. Med. **27**:126, 1947.

18. Friedberg, C. K., and Horn, H.: Acute Myocardial Infarction Not Due to Coronary Artery Occlusion, J. A. M. A. **112**:1675 (April 29) 1939.

19. Moritz, A. R., and Atkins, J. P.: Cardiac Contusion: An Experimental and Pathological Study, Arch. Path. **25**:445 (April) 1938.

feature, the resulting myomalacia might well be due to coronary insufficiency secondary to shock, and not to either direct injury of the muscle or occlusion of a coronary artery. The problem of differentiating infarction due to direct injury from that secondary to arterial disease becomes the more difficult as the time interval between injury and postmortem examination is lengthened. For its concise presentation, the summary of Moritz and Atkins [19] is quoted in full:

> The objective pathologic criteria for distinguishing between a cardiac contusion and a cardiac infarct vary in usefulness according to the age of the lesion. In the case of a recent myocardial lesion, the only evidence that should almost invariably serve to identify an otherwise indeterminate injury as an infarct is the finding of recent coronary occlusion. Pathologic changes more likely to be found in early contusion than in early infarction include massive interstitial hemorrhage, laceration and tissue disorganization. Since all of these changes may be seen following spontaneous rupture of an early infarct, they are not conclusive. In the case of an older myocardial lesion there is no means of distinguishing objectively between contusion and infarction. Deposits of hemosiderin in myocardial scars are more likely to be seen in healed contusions than in healed infarcts, but since hemosiderin is seen occasionally in healed infarcts its presence is not conclusive. Three months after injury hemosiderin is found infrequently in traumatic scars, so that its absence in no way excludes the possibility of a lesion having been of traumatic origin. The presence or absence of remote coronary occlusion does not serve to identify a myocardial scar as having resulted from infarction or contusion inasmuch as a heart the seat of occlusive coronary disease may have a superimposed traumatic lesion and a heart with a large healed infarct may have no demonstrable coronary occlusion. The pathologic characteristics of the scars of myocardial contusion and infarction are frequently identical, and the presumptive nature of their origin must be determined by historical data rather than by postmortem examination.

In the case here reported, clinical data obtained before the accident, as well as results of detailed clinical and postmortem studies made after the injury, were available. The trauma appeared to cause direct injury to a large plaque in the descending branch of the left coronary artery, followed by hemorrhage within the plaque and then seepage of blood through the intimal lining (fig. 6) with the development of a thrombus at this site. The early onset of pain in the chest, as well as the results of electrocardiographic examination, indicated that this process must have developed rapidly, with the end stage of occlusion and consequent infarction occurring within a short time after the injury.

The rarity of undoubted traumatic coronary thrombosis is readily confirmed by reference to reports on traumatic and accidental deaths. Hawkes [20] in 1935 reviewed the protocols for a ten year period, 1925 to 1934, of all deaths recorded in the Office of Chief Medical Examiner, in Essex County, N. J. Autopsy was performed in 7,000 cases for medicolegal reasons; of these 2,708 were of traumatic deaths, of which

20. Hawkes, S. Z.: Traumatic Rupture of the Heart and Intrapericardial Structures, Am. J. Surg. **27**:503, 1935.

70 were instances of injury to the heart and great vessels. In only 4 cases was the cardiac injury alone responsible for death. In none was traumatic coronary thrombosis observed. In 262 cases reported by Osborn,[21] who studied the observations made on persons in fatal accidents, no reference to direct damage to the coronary arteries was included.

Contusion to the heart must be entertained not only in those instances of external evidences of injury but whenever the possibility exists that the heart was traumatized by a blow to the chest, even in the absence of signs of external violence. Discoloration due to bruising of the skin and subcutaneous tissues may not be demonstrable immediately after the accident. The mechanism of contusion by sudden jarring of the heart against the interior of the bony thorax when parts of the body distant from the chest are struck must also be kept in mind.

Clinical symptoms vary considerably in injury to the chest and heart. While the dramatic evidences of shock, with collapse, air hunger, restlessness and pallor, may be present, oftener symptoms are less obvious and so unobtrusive that patients are allowed their usual activity, only to die suddenly from rupture of the heart during the period of softening of the contused muscle. Patients usually do not faint. In Warburg's latest group of 59 cases,[9] fainting was specified in only 4 instances, while in 24 the absence of fainting was explicity mentioned. In 10 of this group a latent period of a few days to several months intervened between the time of accident and the appearance of clinical symptoms. Barber [22] stated that in his experience a latent period is the rule rather than the exception, as he observed symptomless intervals of twelve hours to three days.

Pain may be a complaint immediately after or at some time subsequent to the accident. It is frequently difficult to differentiate the pain arising in a contused chest wall from that having its origin in bruised cardiac muscle. Shortly after injury, pain may be prolonged and severe in both. Later, the pain of a contused chest tends to be more constant and may last for several days, abating slowly. It is significant that in Warburg's series of 51 cases which were considered to be definitely of traumatic origin on postmortem examination 15 showed no symptoms immediately after the accident to suggest the possibility of injury to the heart.[8] A slight rise in temperature or an increased rate of sedimentation of the red blood cells may serve to indicate the presence of bruised muscle tissue.

21. Osborn, G. R.: Findings in Two Hundred Sixty-Two Fatal Accidents, Lancet **2**:277, 1943.

22. Barber, H.: The Effects of Trauma Direct and Indirect, on the Heart, Quart. J. Med. **13**:137, 1944.

Serial electrocardiograms taken immediately after trauma are indispensable to the diagnosis of cardiac contusion. Electrocardiographic abnormalities may be transient, lasting but a few days. Barber [22] did routine electrocardiograms on all patients admitted with a history of accident, if they were seen within forty-eight hours. Among 75 unselected patients, 20 showed abnormal electrocardiographic tracings. In 1 patient there was no postmortem evidence of myocardial bruising twelve days after the T waves in leads I and II had been flat or slightly inverted. In another patient permanent partial heart block was present. In 17 instances the electrocardiograms returned to normal in a short time, indicating that these abnormalities were the result of the trauma. Such temporary abnormalities were recorded most frequently one or two days after injury. On several occasions, the electrocardiogram, normal a few hours after the accident, showed abnormalities twenty-four or forty-eight hours later. In the severer contusions, electrocardiographic abnormalities similar to those seen in coronary disease with occlusion may occur. Thus, Kissane [23] observed that the changes in the RS-T complex and in the T waves frequently do not occur for twenty-four to forty-eight hours, but that they are similar in every respect to those changes characteristic of coronary occlusion. He also emphasized the importance of repeated electrocardiograms in cases of trauma.

Anderson,[24] in reviewing nonpenetrating injuries of the human heart, stated that the electrocardiographic tracings in 30 cases in which abnormalities had been described were in accord with experimental data. The T waves may be unusually large or inverted. The RS-T complex may be either elevated or depressed. Typical coronary T waves may occur and are similar to those observed in coronary thrombosis and in pericarditis with or without effusion. Q waves may be abnormally deep, and the QRS complex may show slurring and notching. The frequency of involvement of the muscle just under the pericardium may account for the same kind of changes in the RS-T complex as are seen in coronary occlusion with infarction.

SUMMARY

A rare instance of thrombosis of a major coronary artery, with consequent myocardial infarction due to contusion of the wall of the chest, is described. The historical, clinical and pathologic data presented leave little doubt as to the role of blunt injury to the chest in producing the lesion described in this case.

1185 Park Avenue (28).

23. Kissane, R. W.: Cardiac Contusion, in Blumer, A.: The Practitioners Library of Medicine and Surgery, 1940 supplement, New York, D. Appleton-Century Company, Inc., p. 318.

24. Anderson, R. G.: Non-Penetrating Injuries of the Heart, Brit. M. J. **2**:307, 1940.

CHRONIC NONLEUKEMIC MYELOSIS

Report of Six Cases

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THE NAME "chronic nonleukemic myelosis" seems the most appropriate for certain conditions which have been described in hematologic literature under a wide variety of other names. The term (Mavros; Hickling; Carpenter and Flory [1]) is, in the main, merely descriptive, and not even particularly accurate. Other suggested names for the syndrome include "chronic splenomegaly with anaemia and myeloid reaction of the blood" (Emile-Weil and Clerc [2]); "splenomegaly of the myeloid type without myelocythemia" (Rathery [3]); "myeloid megakaryocytic splenomegaly" (Downey and Nordland [4]); "splenomegaly with myeloid transformation" (Tudhope [5]); "hepatolienal hematopoietic endotheliosis" (Lindeboom [6]), and "agnogenic myeloid metaplasia" (Jackson, Parker and Lemon; Reich and Rumsey [7]). All

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1. (*a*) Mavros, A.: Folia haemat. **43**:323, 1931. (*b*) Hickling, R. A.: Quart. J. Med. **6**:253, 1937. (*c*) Carpenter, G., and Flory, C. M.: Chronic Nonleukemic Myelosis: Report of Case with Megakaryocytic Myeloid Splenomegaly, Leukoerythroblastic Anemia, Generalized Osteosclerosis and Myelofibrosis, Arch. Int. Med. **67**:489 (March) 1941.

2. Emile-Weil, P., and Clerc, A.: Semaine méd. **22**:373, 1902.

3. Rathery, F.: Compt. rend. Soc. de biol. **54**:138, 1902.

4. Downey, H., and Nordland, M.: Folia haemat. **62**:1, 1939.

5. Tudhope, G. R.: J. Path. & Bact. **44**:99, 1937.

6. Lindeboom, G. A.: So-Called Aleukemic Megakaryocstic Myelosis, Nederl. tijdschr. v. geneesk. **82**:3072, 1938; abstracted, J. A. M. A. **111**:664 (Aug. 13) 1938.

7. Jackson, H., Jr.; Parker, F., Jr., and Lemon, H. M.: New England J. Med. **222**:985, 1940. Reich, C., and Rumsey, W., Jr.: Agnogenic Myeloid Metaplasia of Spleen: Report of Five Cases Illustrating Diagnostic Difficulties and Danger of Splenectomy and Radiation Therapy, J. A. M. A. **118**:1200 (April 4) 1942.

the names referred to a condition in which there may or may not be anemia, but in which there are usually primitive red and white cells in the peripheral blood, though the great increase in leukocytes characteristic of leukemia is usually absent. The spleen is enlarged, and, at autopsy, foci of extramedullary hemopoiesis may be found in the spleen and liver and to a lesser extent in other organs, such as the kidneys and the lymph nodes. There also are recorded a number of cases of essentially similar conditions, associated with myelosclerosis and myelofibrosis and described as "fibrosis of the bone marrow associated with a leukemoid blood picture" (Mettier and Rusk; Rosenthal and Erf [8]); "myelophthisic splenomegaly" (Ballin and Morse [9]); "megakaryocytic myelosis with osteosclerosis" (Hewer [10]), and "aleukemic myelosis with osteosclerosis" (Stephens and Bredeck [11]). In some cases primitive red and white cells were not reported in the peripheral blood, but it is possible that the blood had not been examined on the number of occasions which McMichael and McNee,[12] in 1936, showed to be essential for the diagnosis. A similar clinical picture was also described by Vaughan,[13] in 1936, as a "leuco-erythroblastic blood picture," associated with osteosclerosis, myelofibrosis, and with metastasis to bone from malignant tumors, Hodgkin's disease and multiple myelomatosis. In some cases in which autopsy was performed, there was massive myeloid metaplasia of the spleen. In others, the masses were collected into tumor-like nodules and, because of the predominance of megakaryocytes, the condition was called megakaryocytoma of the spleen (Downey and Nordland [4]). Sometimes the giant cells have been present in such numbers as to form a most striking feature. They have been found in the spleen, liver, bone marrow and lymph nodes.[14] Extramedullary hemopoiesis has also been observed in other conditions, including pernicious anemia, anemia of severe sepsis, repeated bleeding and many varieties of hemolytic anemia (Wintrobe [15]). An interesting report on a case of hemolytic anemia was recently published by Brewster

8. Mettier, S. R., and Rusk, G. Y.: Am. J. Path. **13**:377, 1937. Rosenthal, N., and Erf., L. A.: Clinical Observations on Osteopetrosis and Myelofibrosis, Arch. Int. Med. **71**:793 (June) 1943.

9. Ballin, M., and Morse, P. F.: Myelophthisic Splenomegaly, J. A. M. A. **89**: 1671 (Nov. 12) 1927.

10. Hewer, T. F.: J. Path. & Bact. **45**:383, 1937.

11. Stephens, D. J., and Bredeck, J. F.: Ann. Int. Med. **6**:1087, 1933.

12. McMichael, J., and McNee, J. W.: Edinburgh M. J. **43**:303, 1936.

13. Vaughan, J. M.: J. Path. & Bact. **42**:541, 1936.

14. Hickling,[1b] Rathery,[3] Tudhope,[5] Ballin and Morse,[9] Downey, D.; Palmer, M., and Powell, L.: Folia haemat. **41**:55, 1930. Hirsch, E. F.: Generalized Osteosclerosis with Chronic Polycythemia Vera, Arch. Path. **19**:91 (Jan.) 1935.

15. Wintrobe, M. M.: Clinical Hematology, ed. 2, London, Henry Kimpton, 1946.

and Wollenman.[16] The uniform absence of real leukemic infiltrations and the multiplicity of cell types involved in the metaplasia were said to distinguish the condition from true leukemia. The association of pronounced erythropoiesis and leukopoiesis with proliferation of giant cells distinguished the condition from that described by others (Stengel; Wilson; Kettle; Ross[17]), in which there was proliferation of giant cells only (Vaughan and Harrison[18]). In these two types, it was not always possible to determine whether or not myelosclerosis or myelofibrosis was associated, but it is striking that patients with massive myeloid splenomegaly and osteosclerosis showed the same variations in the duration of the disease and in the type of blood picture as did those with myeloid splenomegaly without osteosclerosis. In both groups, there were acute and chronic cases; in both groups, immature cells were usually present in the circulating blood, though rarely they were not, and in both groups, the blood could be said to have been "leukemic," that is, there was often a great increase in the number of circulating leukocytes, a high proportion of which were frequently immature (Hickling[1b]).

I have been able to study 6 cases of this syndrome, in 2 of which autopsy reports were at my disposal. Available hematologic data in these cases, with reports of examinations of the bone marrow, are given after the case histories.

REPORT OF CASES

CASE 1.—*History.*—A white woman of 65 was first seen in 1943, when she complained of a lump in the left side of the abdomen. She stated that she had been aware of the lump for at least five years. It had never actually been painful, but it appeared to be increasing gradually in size and had recently become uncomfortably large. The patient had no cough, but she had lost about 20 pounds (9.1 Kg.) in the previous few months. She had also felt a little weaker and had experienced some dyspnea on exertion. There was a history of an itchy cutaneous eruption, not unlike urticaria. It had lasted a few days and had then disappeared. The previous history was noncontributory. The patient had never had malaria.

Examination.—The general condition of the patient was good. The mucous membranes were reasonably well colored, and there was no obvious loss of weight. The cardiovascular system was apparently normal. The blood pressure was 160 systolic and 90 diastolic. There were no murmurs.

The spleen was enlarged, extending almost into the left iliac fossa, and was firm and not tender. The liver was also firm and extended 3 fingerbreadths below the costal margin; it was not tender. There were no enlarged lymph nodes. The

16. Brewster, H. H., and Wollenman, O. J.: New England J. Med. **227**:822, 1942.

17. Stengel, A.: Tr. A. Am. Physicians **19**:174, 1904. Wilson, L. B.: Surg., Gynec. & Obst. **16**:240, 1913. Kettle, E. H.: J. Path. & Bact. **23**:413, 1920. Ross, J. M.: J. Path. & Bact. **37**:311, 1933.

18. Vaughan, J. M., and Harrison, C. V.: J. Path. & Bact. **48**:339, 1939.

urine was normal, and there were no significant findings in any of the other systems. The result of the examination of the bone marrow was reported as normal.

Course.—The patient was subsequently readmitted to the hospital on a number of occasions; the only notable additional symptoms were episodes of pain in the right loin and associated hematuria. In addition, the spleen had increased still further in size, almost to the point of entering the pelvis. Irradiation of the spleen was begun in 1945, when 3,975 r were given in three months. In 1946, 4,225 r were given, centering over the lumbar spine, and in 1947, 925 r were directed to the spleen. The therapeutic maneuvers resulted in a decrease in the size of the spleen (it then extended about 3 fingerbreadths below the umbilicus) and depressed the level of the white cell count. The dragging weight of the spleen became less severe.

The patient grew gradually weaker during 1947 and complained of severe pain in the right loin and of dysuria. Albumin and blood were present in the urine. The patient died during July 1947. The blood (tables 1 and 2) at no time showed any anemia, but there was a gross increase in polymorphonuclear leukocytes in the peripheral blood; thrombocytosis and occasional normoblasts were noted. A second examination of the bone marrow also indicated that it was normal and not leukemic.

Autopsy (performed by Dr. G. Selzer nine hours after death).—The lymph nodes were not enlarged. The spleen weighed 1,342 Gm. It showed extensive "sugar icing" of the capsule and was adherent to the liver; it was moderately soft. The cut surface was gray-pink in color and resembled the spleen in cases of chronic myeloid leukemia. The liver weighed 2,560 Gm. and showed cloudy swelling only. The right femur showed hyperplastic gray-pink marrow throughout its entire length, as did the right tibia up to a point 2 inches (5 cm.) from its distal extremity. The sternum showed similar gray-pink marrow. The lungs showed multiple pyemic abscesses and a recent infarct. The right kidney was large, weighed 410 Gm. and showed extensive chronic suppuration involving almost all the kidney. There was a large amount of yellow gravel. The other kidney was normal.

Histologic Examination.—Spleen: The pulp was largely converted into myeloid tissue, showing all stages of cell development from myeloblasts to mature, segmented polymorphonuclear leukocytes, the latter predominating. Megakaryocytes were present but were scanty. There was no lymphoid tissue left in the organ.

Bone Marrow: The bone marrow showed extensive myeloid hyperplasia, which had completely replaced the fat of the marrow. Megakaryocytes were numerous. There was no fibrosis. The marrow cells were mainly myelocytes, but there were scattered "myeloblast islands." Immature cells were more numerous than the more mature forms of the myeloid series. The condition of the marrow was consistent with that in true myeloid leukemia.

Liver: The liver showed cloudy swelling and scanty myeloid infiltration in the sinusoids. The cells were predominantly polymorphonuclear leukocytes, but occasional immature cells were also present. Megakaryocytes were not obvious. Only occasional abnormal cells were found in the portal tracts.

Lungs: The lungs showed foci of suppuration. There were large numbers of myeloid cells and numerous megakaryocytes in the capillaries.

Kidneys: Only foci of suppuration were noted in the kidneys.

Other Organs: None of the other organs showed striking changes. Most of the organs showed myeloid cells in the capillaries, but the development was

not so pronounced as in the lungs, nor were megakaryocytes demonstrable in organs other than the spleen or lungs.

Postmortem Diagnosis.—The diagnosis was chronic leukemia, with splenomegaly and hyperplasia of the marrow. In addition there were suppurative pyelonephritis due to calculus and terminal pyemia.

CASE 2.—*History.*—A white man of 76 was admitted to the hospital after an episode of superficial sepsis of the second, third and fourth fingers of the left hand, acquired during a voyage from the Netherlands to Capetown. The local lesion was incised and soon resolved. At the same time the patient stated that he had had a little hematuria; as in addition he had fever, he was hospitalized for further investigation. Since his ship had called at Freetown, Sierra Leone, and since he had a history of malaria forty years previously, it was considered possible that he had malaria. The only other significant factor in the history was that of intermittent episodes of classic gout, which the patient had had for the past twenty years.

Examination.—The patient was a surprisingly young-looking man, with a highly colored complexion. There was no jaundice, clubbing of the fingers or cyanosis. There were healing ulcers on the tips of the third and fourth fingers of the left hand. No abnormalities were detected in the cardiovascular system; there was no cardiac enlargement. Blood pressure was 124 systolic and 60 diastolic. The spleen was palpable 3 fingerbreadths below the costal margin. Its surface was smooth, and it was firm, with a sharp edge. The liver was also palpable 3 fingerbreadths below the costal margin and was also firm and smooth. No abnormalities were present in the other systems. There were no palpable lymph nodes. The urine was normal. Repeated search for malaria parasites proved unsuccessful. The pyrexia gradually subsided; cause for it was never adequately established. The level of blood uric acid was 4.0 mg. per hundred cubic centimeters. The blood count (tables 1 and 2) almost reached the level for polycythemia, and there was a great increase in cells of the myeloid series. The differential bone marrow count (table 3) indicated a myeloid reaction, the number of myelocytes being in the upper level of the normal range. Roentgenologic studies of long bones revealed no abnormalities.

Course.—The patient was transferred to the outpatient department, where he received a total of 172 r in body baths over the next three months. Three months after the roentgen therapy was completed, he had a typical episode of gout, which was no different from those he had experienced previously, and which gradually subsided.

Three months later he noticed coldness and blueness of the terminal portions of the two medial toes of the right foot; he had also experienced an episode of "pins and needles" in the foot. He was readmitted to the hospital for further investigation. The spleen then extended only 1 fingerbreadth below the costal margin, and the liver was unaltered. The blood findings were also essentially the same. Local examination of both legs disclosed symptoms consistent with organic occlusion to the vessels of both feet. There was definite cyanosis of the tips of the toes, depending on room temperature, and both feet were cold. Skin temperatures were: right foot, 22 to 23 C.; left foot, 24 to 25 C.

The plethysmographic examination, made by Prof. R. H. Goetz, indicated that pulse volume during full dilatation was 0.005 cc. (normal volume is 0.02 cc.). Rate of flow was larger than one would have expected, the reduction in pulse volume indicating a relatively well developed collateral circulation. The level of

blood uric acid was 6.7 mg. per hundred cubic centimeters. Blood pressure was 160 systolic and 90 diastolic. The patient was treated by intermittent venous occlusion and lumbar diathermy, and papaverine was administered. He improved for a while, but the local condition recurred, and he was submitted to lumbar sympathectomy. Unfortunately, severe wound sepsis due to a penicillin-resistant streptococcus developed, and the patient died about three weeks after the operation.

Autopsy (performed by Dr. G. Selzer).—Owing to legal delays the autopsy could not be performed until thirty-six hours after death. The organs all showed considerable postmortem change. There was atheroma of the right and the left coronary artery; the left one was completely occluded about 3 cm. from the coronary orifice. The liver weighed 1,700 Gm. The kidneys were somewhat scarred, and there was gravel in both renal pelves. The spleen was greatly enlarged and weighed 755 Gm. The bone marrow was extremely hyperplastic. The whole of the femur was replaced with red marrow, as was the upper 2 inches (5 cm.) of the tibia. There was, however, a diffuse overgrowth of the marrow with bony trabeculae. There were no enlarged lymph nodes.

Histologic Examination.—Microscopically, none of the viscera except the spleen showed infiltration with myeloid cells. In the liver there were very scanty groups of cells in the portal tracts. The spleen showed considerable postmortem change. The lymph follicles were, however, still recognizable. There was considerable infiltration of myeloid cells, mainly polymorphonuclear leukocytes, in the splenic pulp. The condition of the bone marrow did not differ essentially from that seen during life, with the exception of the presence of osteosclerosis.

Postmortem Diagnosis.—There was considerable myeloid hyperplasia in the spleen and bone marrow, associated with osteosclerosis. There was no "true leukemia."

CASE 3.—*History.*—A white man of 62 had been well until about seven years previous to examination, when he had begun to experience recurrent episodes of acute arthritis. These started in the right big toe, which was acutely tender and painful. After a month of almost continuous pain in this toe, the big toe of the left foot became involved in a similar manner. The affected joints remained swollen and painful for a further two months, at which time the disorder gradually subsided, leaving no residual joint disturbance or deformity. Several months later, the patient had further episodes of classic gout, which gradually involved more and more joints and eventually left deformity. The metatarsophalangeal joint, the carpal joints and the wrists, knees and elbows all became involved. Contributory data were not obtained from the previous history or from the family history, except for trauma of the right elbow and the left wrist years previously.

Examination.—The patient had a highly colored complexion, with superficial telangiectases on the face. The mucous membranes were well colored.

Both the right elbow and the left wrist were deformed as a result of trauma. In addition, all the joints of both hands were deformed as a result of arthritis, and there was fusiform swelling of the joints of the fingers, with limitation of movement. The knees and the joints of both feet were swollen and deformed, as were the small joints of the toes. There was bursitis of the left olecranon. In addition, gouty tophi were present around the knees and the left elbow.

No cardiac enlargement was noted. The pulse was grossly irregular, due to auricular fibrillation. The vessels were arteriosclerotic. No murmurs were heard in the heart. Blood pressure was 115 systolic and 65 diastolic.

The spleen was greatly enlarged and extended about 5 inches (12.5 cm.) below the costal margin. It was firm, smooth and not tender, as was the liver, which was palpable about *2* fingerbreadths below the costal margin. No other masses were palpable. The other systems were normal.

The urine was normal. The level of serum uric acid was 8.5 mg. per hundred cubic centimeters. A biopsy specimen from one of the tophi showed the classic histologic features of gout. Sodium urate crystals were also demonstrated. The blood count (tables 1 and *2*) almost reached the level for polycythemia. In addition, there were thrombocytosis and a gross increase in mature myeloid cells. The bone marrow (table 3) showed both myeloid and erythroid hyperplasia, with relatively scanty primitive myeloid cells.

Course.—The patient responded to the usual therapy for gout and was discharged as reasonably fit. He is still alive and well at the time of writing.

Diagnosis.—The diagnosis was gout associated with chronic nonleukemic myelosis.

CASE 4.—*History.*—A white woman of 64 had had malaria thirty-six years previously, with numerous recurrences for sixteen years, after which she had been free of the disease. About six years after the first episode of malaria, the spleen was found to be enlarged; the patient had been aware of a lump in the left loin for a great many years. Four years after the discovery that the spleen was enlarged, laparotomy was performed, and the diagnosis was confirmed. The patient stated that a "tumor" of the stomach was removed at the same time. Ever since the operation she had had intermittent episodes of diarrhea, lasting for one or two weeks and then clearing up for some months, only to recur. No cause for the diarrhea was found. During the episodes she passed up to ten stools per day, containing blood and mucus. For the last few years she also had had a severe dragging feeling in the left flank. One sister had polycythemia vera, and 1 brother had trouble with the "spleen"(?).

Examination.—The mucous membranes were pale. The cardiovascular system was normal; blood pressure was 150 systolic and 60 diastolic. The spleen was grossly enlarged, extending to a point 4 fingerbreadths below the umbilicus. It was smooth and firm, with a sharp edge, and was slightly tender. The liver extended 3 fingerbreadths below the costal margin and was firm, smooth and not tender. The urine was normal. The blood showed anemia, a constant increase in reticulocytes and an associated increase in polymorphonuclear leukocytes. No bone marrow could be obtained, even on repeated attempts. Roentgenoscopic examination of the gastrointestinal tract and examination of the stools failed to reveal the cause of the diarrhea. The patient was discharged unimproved; she is still alive at the time of this report.

Diagnosis.—The diagnosis was possible chronic hemolytic anemia as a relic of malaria. The diagnosis of osteofibrosis of bone marrow was indefinite.

CASE 5.—*History.*—A white man of 74 had had anginal pain on moderate exertion for the past ten years, as well as a feeling of tiredness and lack of energy. The symptoms had been no worse in recent years. In addition, he had episodes of what he described as a hot feeling in the body, enough to make him "want to throw the blankets away," and usually occurring about *2* a. m. The episodes were relieved by his getting out of bed. They were not associated with dyspnea.

For about eight years, the patient had had an itchy rash, covering most of the body. The rash was associated with edema of the hands and face; on one occasion the eyelids were particularly affected. The rash consisted of crops of

small, reddish papules, occurring chiefly on the arms and legs but also extending onto the body; it lasted a few weeks and then faded, being followed with desquamation. The episodes had recurred every few weeks or months. The patient also had had episodes of burning and itching of the eyes. He was admitted to the hospital because his physician had palpated an enlarged liver.

Previous History and Family History.—Cholecystectomy had been performed sixteen years previously. There had been considerable indulgence in alcohol up to nine years before the hospitalization of the present report. Many members of the patient's family had "eczema." One sister died of "pernicious anemia."

Examination.—The patient was a healthy-looking man with a rather florid skin. There was pronounced palmar erythema, but no rash was present. No lymph nodes were palpable.

The edge of the liver was felt 3 fingerbreadths below the costal margin. It was firm, smooth and not tender. The spleen was just felt beneath the left costal margin and was firm and smooth. No other abdominal masses were felt.

The heart was not clinically enlarged. The blood pressure was 160 systolic and 80 diastolic. The urine was normal. Results of numerous tests for liver function were within normal limits. The level of serum uric acid was 5.4 mg. per hundred cubic centimeters. Roentgenograms of the chest, femurs, humeri, vertebrae and pelvis were normal and revealed no evidence of osteosclerosis. The blood showed slight anemia, with a gross increase of mature myeloid cells; however, numerous band forms were included. The bone marrow showed myeloid hyperplasia, with a slight increase in myelocytes. The patient was discharged unimproved.

Diagnosis.—The diagnosis was chronic nonleukemic myelosis. The presence of chronic myeloid leukemia was not proved.

CASE 6.—*History.*—A white man of 57 had been well until about three years prior to admission to the hospital, when he began to experience recurrent headaches. These were severe, were situated on the vertex and occurred at no particular time. They were not associated with visual auras. Two years before admission, while walking, the patient had suddenly noticed a weakness in the right arm and leg, and associated difficulty with speech. The condition became worse for about twelve hours, by which time he had complete right hemiplegia and almost complete aphasia. A year elapsed before he recovered full use of the right side of the body and of speech.

Prior to admission he had had a dragging feeling in the left side of the hypochondrium. The pain was aggravated by his assuming the erect posture and relieved by his "lifting the abdomen up" with his hand. The patient had had malaria many years before, the last episode having occurred twenty-seven years previous to admission. Other family and personal history was noncontributory.

Examination.—The patient's general condition was good. The lymph nodes were not enlarged. There were varicose veins in both legs, with areas of induration and pigmentation, and slight erythema of the lower parts of the legs and the dorsa of the feet, with scaly desquamation of the skin.

The liver was palpable 1 fingerbreadth below the costal margin, of normal consistency and not tender. The spleen was very large and extended down to the umbilicus. Its edge was well defined and sharp; the surface was slightly lobulated, and of firm consistency. The spleen was slightly tender. The prostate gland was soft and was not enlarged.

No cardiac enlargement was noted. The blood pressure was 170 systolic and 115 diastolic. There were residual signs of weakness of the right side of the body, and some increase in tone. The right plantar reflex was more nearly extensor

than flexor in type, but not definitely extensor. There was no sensory loss. The urine was normal. Results of chemical analyses of the serum were: inorganic phosphorus, 3.4 mg. per hundred cubic centimeters; alkaline phosphatase, 11.4 Bodansky units; acid phosphatase, 3.1 Bodansky units; uric acid, 10.2 mg. per hundred cubic centimeters; thymol turbidity reaction, 4; thymol flocculation, 3; colloidal gold, 3; van den Bergh reaction, negative; there was only a minute trace of bilirubin. The level of blood urea was 37 mg. per hundred cubic centimeters. Roentgenograms of long bones showed no evidence of pathologic states. The blood showed slight anemia, with a gross myeloid reaction; numerous myelocytes were present. The bone marrow, however, showed a mature type of myeloid

TABLE 1.—*Erythrocytes and Thrombocytes in the Peripheral Blood in Chronic Nonleukemic Myelosis*

Case	Erythrocytes, Millions per Cu. Mm.	Hemoglobin, Gm. per 100 Cc.	Volume of Packed Cells, Percentage	Reticulocytes, Percentage	Thrombocytes, Millions per Cu. Mm.
1	4.97	14.7	43.0	1.8	1.5
2	5.85	16.6	55.0	1.0	0.76
3	6.50	17.8	51.5	2.4	1.7
4	3.25	8.1	23.0	5.0	0.41
5	3.94	13.3	43.0	3.0	0.197
6	3.20	13.5	39.0	...	0.577

TABLE 2.—*White Blood Cells in the Peripheral Blood in Chronic Nonleukemic Myelosis*

		Polymorphonuclear Leukocytes, %									
		Mature Cells				Immature Cells					
Case	Leukocytes, Total per Cu. Mm.	Neutrophils	Eosinophils	Basophils	Band Forms	Myelocytes	Myeloblasts	Total Cells	Lymphocytes, %	Monocytes, %	Red Cell Series, %
1	33,400	90.0	2.0	0	0	1.0	0	93.0	5.0	2.0	1.0
2	26,000	63.0	0	0	0	18.0*	0	81.0	19.0	0	0
3	24,000	80.0	4.5	1.5	4.0	0	0	90.0	10.0	0	0
4	14,000	78.0	0	0	...	0	0	78.0	16.0	6.0	0
5	44,250	71.5	2.75	2.75	15.0	5.0	0	97.0	2.0	1.0	3.0
6	93,550	52.5	0	2.0	21.0	19.0	0	94.5	5.0	0.5	1.0

* The cells in this case, which were not classic myelocytes, resembled monocytes in many respects.

hyperplasia, with relatively scanty myelocytes and more primitive cells. The patient was discharged unimproved.

Diagnosis.—The diagnosis was chronic nonleukemic myelosis. The diagnosis of chronic myeloid leukemia was indefinite.

STUDIES OF BONE MARROW SECTIONS

CASE 1.—The marrow was studied by others during life and reported as nonleukemic. At autopsy, the marrow was consistent with leukemic marrow.

CASE 2.—Gross nonleukemic myeloid hyperplasia was demonstrated during life in sections made from aspirated sternal marrow. Active marrow was also obtained from the femur during life (Merskey[19]). No osteosclerosis or osteofibrosis was demonstrated in the sections obtained during life. At autopsy, however, pronounced overgrowth of the marrow with bone trabeculae was demonstrated.

19. Merskey, C.: South African M. J. **23**:166, 1949.

CASE 3.—Gross nonleukemic myeloid hyperplasia was demonstrated during life in sections made from aspirated sternal marrow. No osteosclerosis or osteofibrosis was demonstrated in the sections.

CASE 4.—No marrow was obtained, even after repeated attempts; it was possibly fibrotic. Trephinement was not attempted.

CASES 5 AND 6.—Mild nonleukemic myeloid hyperplasia was demonstrated during life in sections of aspirated sternal marrow; "hyperplasia in extension" [19] was shown in specimens of the marrow of the femur. The sternal marrow in these 2 cases did not seem to be so grossly hyperplastic as that in the first 3 cases.

Megakarocytes were numerous in all cases.

TABLE 3.—*Differential Bone Marrow Counts in Chronic Nonleukemic Myelosis*

	Cases			
	2	3	5	6
	White Blood Cell Series, %			
Myeloblasts	1.0	0.66	0.25	0.75
Premyelocytes	1.0	1.33	2.25	1.75
Myelocytes	29.0*	10.0	16.25	8.50
Metamyelocytes	5.0	10.0	18.5	11.5
Eosinophilic myelocytes	0	0.33	0.75	0
Band forms	18.0	16.0	9.75	22.25
Polymorphonuclear leukocytes				
Neutrophils	40.0	29.0	42.25	49.0
Eosinophils	1.0	0.33	0.75	0
Basophils	0	0.33	0.75	0.5
Lymphocytes	2.0	6.0	5.25	3.0
Monocytes	0	0.66	0	0.5
	Red Blood Cell Series, %			
Erythroblasts	0	1.0	0	0.25
Late erythroblasts	1.0	12.66	0	1.0
Normoblasts	2.0	11.66	3.25	1.0
Myeloid: erythroid ratio	31.7:1	2.83:1	28.2:1	41.8:1

* The cells in this case, which were not classic myelocytes, resembled monocytes in many respects.

COMMENT

Clinical Picture.—There was nothing particularly characteristic about the clinical picture. All the patients were elderly, and in all cases the disease followed a somewhat symptomless course. The chief symptoms were of a general nature, such as vague feelings of ill health and lack of strength. A feeling of a heavy weight in the left loin was commonly encountered. Usually the general symptoms were related to the degree of anemia. A previous history of malaria was encountered in 3 of the 6 cases, but in all cases the last episode had occurred at least twenty years prior to examination. It was impossible to assess the importance of this factor, but it seemed to be relatively minor. Certainly there was no evidence of active malaria. With the exception of gout, all the other symptoms could have been fortuitous in patients of such an age, as they were mainly cardiovascular in nature. The association

of gout with this clinical syndrome is interesting. It has long been realized that there is an association between gout and leukemia (Vining and Thomson; Forkner; Lambie [20]); between gout and remissions of pernicious anemia induced by the administration of liver, even when the liver extract used is purine free (Riddle; Opsahl; Morlock and Rosenberg [21]); between gout and types of hemolytic anemia (Lambie [20c]), and between gout and polycythemia vera (Isaacs; Davis; Weber; Tinney and others [22]). It has been generally assumed that the hyperuricemia is due to excessive maturation of the normoblasts or of the leukocytes in the bone marrow. It appears to be related to excessive production of either red or white cells in the bone marrow. Nevertheless, the relation is by no means a constant one; Lambie [20c] suggested that the role of heredity may be of importance in predisposition to the disease. However, in the cases reported in this paper in which gout was associated, there was no history of a familial predisposition. The case reported by Reifenstein [23] as "Erythremia, Gout and Subleukemic Myelosis" appears to parallel the case in this series very closely. There was no real reason to classify the case as one of erythremia, as the evidence for plethora was not satisfactory.

Blood.—In 2 cases the red cell count was normal. A mild degree of anemia was present in 1 case and severe anemia, in another case, whereas in 2 cases the count almost reached the level for polycythemia. However, as I have stated elsewhere,[24] the counts were just below diagnostic levels for polycythemia. The number of reticulocytes was normal in 3 cases, just above normal in 1 case and consistently raised in another case. The high count raised the possibility that the last case was one of chronic hemolytic anemia, possibly a relic of past malaria, which is one of the known causes of the syndrome. Erythrocyte fragility to hypotonic saline solution was normal in this case, and sickling of the red cells could not be demonstrated. The number of thrombocytes was

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20. (*a*) Vining, C. W., and Thomson, J. G.: Arch. Dis. Childhood **9**:277, 1934. (*b*) Forkner, C. E.: Leukemia and Allied Disorders, New York, The Macmillan Company, 1938. (*c*) Lambie, C. G.: M. J. Australia **1**:535, 1940.

21. Riddle, M. C.: J. Clin. Investigation **8**:69, 1929. Opsahl, R.: Acta med. Scandinav. **102**:611, 1939. Morlock, C. G., and Rosenberg, E. F.: Ann. Int. Med. **20**:981, 1944.

22. (*a*) Isaacs, R.: Pathologic Physiology of Polycythemia Vera, Arch. Int. Med. **31**:289 (Feb.) 1923. (*b*) Davis, N. S., III: Polycythemia Vera (Vaquez-Osler Disease): Gout, Angulation of Left Ureter with Beginning Left Hydronephrosis, J. A. M. A. **92**:1595 (May 11) 1929. (*c*) Weber, F. P.: Lancet **2**:808, 1934. (*d*) Tinney, W. S.; Polley, H. F.; Hall, B. E., and Giffin, H. Z.: Proc. Staff. Meet., Mayo Clin. **20**:49, 1945.

23. Reifenstein, G. H.: Am. J. M. Sc. **197**:215, 1939; ibid., **210**:638, 1945.

24. Merskey, C.: To be published.

within the normal range in 4 cases, but in 2 it was 1,500,000 and more per cubic millimeter. In 1 of the latter cases the red cells approximated the level for polycythemia; an increase was thus shown in all the cell elements of the peripheral blood, that is, the red cells, the white cells and the thrombocytes. The white cells were increased in all cases and showed varying degrees of immaturity, associated in 2 of the cases with immaturity of the red cells as well. In none of the cases were myeloblasts present in the peripheral blood, but in all, the cells of the polymorphonuclear leukocyte series were grossly increased, both relatively and numerically. There were, however, no constant correlations between the increases in the red cell series, in the white cell series and in the thrombocytes.

Bone Marrow.—There was no doubt of the hyperplasia of the bone marrow in these cases. Hyperplasia was present *in situ* as well as in extension. Autopsy material demonstrating the hyperplasia was available in 2 cases (cases 1 and 2). In cases 3, 5 and 6, hyperplasia *in situ* was shown in sections of bone marrow taken during life; in cases 5 and 6, hyperplasia in extension was shown in biopsy specimens taken simultaneously from the marrow of the femur.

Curiously enough, in the 2 cases which came to autopsy the extent of the hyperplasia of the marrow was limited and did not occupy the whole length of the tibia. In 1 case it extended to within 2 inches (5 cm.) of its distal extremity, and in the other case it only involved the upper 2 inches of the bone.

Marrow specimens for microscopic study were available in 5 cases. In case 1, results of two examinations of the marrow made during life had been interpreted as not inconsistent with normal marrow; yet, the final conclusion at autopsy was that the marrow was, in fact, leukemic. One of the reasons for the error lay in the fact that the examinations of the marrow during life had been made only on smear preparations; no sections had been prepared from the aspirated marrow particles.[19] Thus, the hyperplasia had been missed. Furthermore, the increase noted in the less mature cells was relatively scanty, even at autopsy, and as the examinations had been carried out several years before death, there may have been an alteration in the marrow picture. Unfortunately, the patient refused a third puncture of the marrow, and the original smears were not available for study.

Adequate marrow sections and smears were available in case 2. In the smears of peripheral blood and of the marrow in this case, there were many atypical cells, which have been classified in the tables as myelocytes, but which were certainly not typical myelocytes. They resembled monocytes in that they had the lobulated, "folded over" nucleus of those cells. There were, however, apparent gradations

between these cells and typical myelocytes. In the marrow there was gross hyperplasia of the myeloid series, as well as osteosclerosis. A curious fact is that hyperplasia of the marrow did not extend to the rest of the tibia. The differential count of the marrow cells in this case demonstrated very little immaturity of the cells, nor did the viscera show infiltration with myeloid cells. Even in the spleen, where there was considerable reaction, the lymph follicles were still preserved.

In cases 3, 5 and 6, the hyperplasia of the marrow was pronounced, but in none of these cases was there much increase in the number of immature cells in the marrow.

The red cell series was practically absent in cases 1, 2, 5 and 6. Despite this fact, it will be noted that the red cell count in case 2 could easily be described as polycythemic. In case 3, in which the red cell count was also high, there were numerous cells of the red cell series in the bone marrow.

Diagnosis.—This rather mixed collection of cases includes 1 case of true chronic myeloid leukemia, 1 case of osteosclerosis with myeloid reaction, 1 case of possible chronic hemolytic anemia (or myelofibrosis) and 3 cases of (possibly) "nonleukemic" myelosis. It was not possible to make a diagnosis during life in the case of osteosclerosis, despite roentgenologic examination of the bones and biopsy of aspirated marrow sections. The diagnosis could perhaps have been made from a section of the sternal marrow obtained by trephination. Chronic hemolytic anemia can usually be diagnosed, but in case 4 the only evidence pointing to that disease was the consistently elevated reticulocyte count. The failure to obtain bone marrow on repeated puncture could perhaps be interpreted as evidence of fibrosis of the marrow; the patient refused to allow trephination to obtain a specimen of the marrow. The real difficulty in diagnosis lay in the differentiation of these disorders from true chronic myeloid leukemia. This factor raised the extremely difficult problem of exactly what is required for a diagnosis of chronic myeloid leukemia. Acute leukemia is usually easy to diagnose, as the examination of the marrow discloses great numbers of immature cells. In less acute cases, however, there are fewer myeloblasts and more myelocytes; in the chronic stages, the cells may become even more mature. It is not possible to lay down exact criteria for diagnosis, to say how many immature cells must be present or how immature the cells must be. Piney and Hamilton-Paterson,[25] for instance, stated that the increase in the cellularity of the marrow in the ordinary chronic stage of the disease depends almost entirely on the increase in the number of myelocytes, which may form as much as

25. Piney, A.; and Hamilton-Paterson, J. L.: Sternal Puncture, ed. 3, London, William Heinemann, Ltd., 1946.

80 per cent of the white cells; a greater increase among cells less differentiated than myelocytes is an indication either of a relapse or that the disease is passing into an acute phase. These authors also stressed the aggregation of cells of a single cell type, such as myelocytes, premyelocytes or myeloblasts. This characteristic, however, can be seen only in thick smears or, better still, in marrow sections, which may be made from the aspirated sternal marrow and which also demonstrate hyperplasia of marrow *in situ*. The hyperplasia in extension may, in addition, be shown by the technic of biopsy of the marrow of the femur.

In the cases described in this series, there was hyperplasia of the myeloid cells both *in situ* and in extension, and aggregations of these cells into groups of a single cell type; yet, there was no true increase in the percentage of immature cells, as judged by generally accepted "normal" standards. Thus, even with all diagnostic aids one may fail to reach a final diagnosis, and even at autopsy the problem may remain unsolved. Some authors stress the finding of leukemic infiltrations outside the bone marrow as necessary for a proved postmortem diagnosis of chronic myeloid leukemia. The spleen is usually involved, and the remaining viscera usually show cellular infiltration. In the liver, for instance, the infiltrations are usually in the portal fields, and not confined to the sinusoids. Judged by these criteria, case 1 would hardly pass for one of chronic myeloid leukemia; it should be classified as one of chronic nonleukemic myelosis; yet, the marrow was definitely leukemic.

The cases of chronic nonleukemic myelosis resemble those of chronic myeloid leukemia in many respects. There was considerable increase in the number of leukocytes, some of which were usually immature; there was hyperplasia of the leukopoietic tissue; there was often an increase in the number of thrombocytes or even of red cells, though there was oftener a normal or lowered red cell count. The great increase and immaturity in the white cells characteristic of true leukemia were usually absent, as were gross leukemic infiltrations at autopsy. Nevertheless, as Heller, Lewisohn and Palin [26] pointed out, the differences are really only in degree and all the differentiating features may be present in greater or lesser degree, or absent in individual cases. The greater the incidence of leukemic features, the worse the prognosis and the greater the disability. The more the condition resembles nonleukemic myelosis, the more chronic the disease and the better the prognosis. In all the cases reported in this series, the disease was chronic in nature. In 5, anemia was either absent or mild in degree, and the disorder in the sixth case may well have been of a differ-

26. Heller, E. L.; Lewisohn, M. G., and Palin, W. E.: Am. J. Path. **23**:327, 1947.

ent etiology. In none of the cases were myeloblasts found in the peripheral blood; even myelocytes were scanty in 4 cases. The total white cell count showed all grades of increase but in general was less than that characteristic of chronic myeloid leukemia. Immature red cells were found only in small numbers in the peripheral blood.

I have discussed elsewhere [24] the true relation between myeloid leukemia and polycythemia vera and concluded that there was a relation through this intermediary group of conditions. The cases reported in this paper lend further evidence to this thesis. Fundamentally all the conditions are related, and they would appear to represent varying degrees of hyperplasia of the hemocytoblast, or whatever one wishes to call the precursory cell of the red cell and white cell series. Should the hyperplasia involve mainly the red cell series, the clinical syndrome of polycythemia vera would result, though even in this disorder considerable proliferation of both the white cell series and the thrombocytes occurs. Should the white cell series be mainly involved with minor degrees of immaturity, chronic nonleukemic myelosis would result; should the degree of immaturity be greater, the condition would be leukemia. Even conditions affecting mainly thrombocytes have been reported [27]; red cells and polymorphonuclear leukocytes were also increased in these conditions. If one cares to go further back, one may say that all the cell types involved, the hemocytoblast, the megakaryocyte, the fibroblast and the osteoblast, were derived from the same primitive mesenchymal reticulum cell of Maximow; the association of all these conditions would then be easy to understand. The start of the hyperplasia is more difficult of explanation, as the stimulus which initiates it is not known.[18] Nevertheless, this hypothesis makes the relation of these diseases easy to understand.

SUMMARY AND CONCLUSIONS

The condition known as chronic nonleukemic myelosis is discussed, and cases of this syndrome are reported. The essential feature of the condition is hyperplasia of the leukopoietic tissues of the body, which results in an increase in the white cell count and in a degree of immaturity in the white cells of the peripheral blood. The bone marrow, especially, shows gross overgrowth of cells of the myeloid series. In addition, varying amounts of myeloid infiltration may be found in other organs, though the degree tends to be slight. Even in the marrow, the hyperplasia appears relatively orderly in nature. Consequently, the marrow does not display the invasive characteristics seen in true leukemia. The course of the condition is prolonged; anemia tends to be slight,

27. Rowlands, R. A., and Vaizey, J. M.: Lancet **2**:1217 (1938). Reid, J.: ibid. **2**:584 (1940).

and disability is often negligible for some years. The bone marrow is not leukemic, in that it does not show immaturity at the myeloblast level, which is characteristic of true leukemia, nor need myelocytes even be very numerous. Nevertheless, the condition may be only a mild variant of leukemia differing only in degree, rather than in any fundamental characteristic.

A similar clinical syndrome may be encountered in myelofibrosis, osteosclerosis, carcinomatosis of bone, myelomatosis or chronic hemolytic anemia. The differential diagnosis may be impossible during life.

The syndrome is also related to polycythemia vera and forms a connecting link between polycythemia vera and true leukemia. It is possible that the syndromes of polycythemia vera, nonleukemic myelosis and true leukemia, and even, possibly, osteosclerosis and myelofibrosis, have a common genesis.

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CHRONIC ULCERATIVE COLITIS AND CARCINOMA

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THE PURPOSE of this communication is to present data on a series of 855 cases of chronic ulcerative colitis, with specific reference to the development of pseudopolyposis and carcinoma.

A review of the literature appears to indicate a growing conviction that carcinoma may develop in patients with chronic ulcerative colitis and pseudopolyposis of long standing. The inference is that the malignant process occurs in the pseudopolyps and in association with, or as the result of, the existing chronic intestinal infection. The reported incidence of such malignant growths varies with different authors. Streicher (1938) [1] reported 1.2 per cent of 217 cases. Matzner and Schaefer (1939) [2] found the incidence of carcinoma among 185 patients with chronic ulcerative colitis to be 1.6 per cent, as compared with 0.5 per cent of the general hospital admissions. Brust and Bargen,[3] in 1934, reported an incidence of 2.5 per cent of 800 cases. In a study of necropsy and biopsy material, they noted transitional phases from chronic ulcerative colitis with pseudopolyposis to adenoma or carcinoma. The next year, Hurst [4] reported polyposis occurring as a complication in 12.5 per cent of 40 patients with chronic ulcerative colitis. Independently of this group, he noted 3 cases of carcinoma, the malignant process in 1 instance developing three years after the patient had completely recovered from ulcerative colitis. Jackman, Bargen and Helmholtz [5] reported carcinoma of the colon in 6.3 per cent of a series of 95 children, as compared with 3.2 per cent in an over-all

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From the Dysentery Registry.

1. Streicher, M. H.: Clinical Course of Chronic Ulcerative Colitis, Am. J. Digest. Dis. **5**:361 (Aug.) 1938.

2. Matzner, M. J., and Schaefer, G.: Chronic Ulcerative Colitis Complicated by Carcinoma, Rev. Gastroenterol. **6**:422 (Sept.-Oct.) 1939.

3. Brust, J. C., and Bargen, J. A.: The Neoplastic Factor in Chronic Ulcerative Colitis, New England J. Med. **210**:692 (March 29) 1934.

4. Hurst, A. F.: Prognosis of Ulcerative Colitis, Lancet **2**:1194 (Nov. 23) 1935.

5. Jackman, R. J.; Bargen, J. A., and Helmholtz, H. F.: Life Histories of Ninety-Five Children with Chronic Ulcerative Colitis: Statistical Study Based on Comparison with Whole Group of Eight Hundred and Seventy-One Patients, Am. J. Dis. Child. **59**:459 (March) 1940.

group of 871 patients with chronic ulcerative colitis. In 1944, Cattell [6] noted intestinal carcinoma in 11 patients with chronic ulcerative colitis of five years' duration or longer. Bargen and Sauer [7] reported 30 additional cases the same year, making a total of 44. Seventeen of the 30 patients had multiple polyps and 9 multiple carcinoma. In a previous study (1929), polyposis had been noted in 10 per cent, and carcinoma in 2.5 per cent, of 693 patients. Ricketts, Benditt and Palmer,[8] in 1945, described carcinoma of the descending colon arising in an area of chronic ulcerative colitis. The patient in this case was 18 years old and had had colitis for fifteen and a half years. The terminal portion of the ileum was also affected. Cattell and Boehme,[9] during a period of seven years, encountered 9 patients with chronic ulcerative colitis and carcinoma, the average duration of the colitis being nine years. In 1946, Ricketts and Palmer [10] reviewed 206 cases of chronic ulcerative colitis: Pseudopolyposis was present in 21 (10 per cent), and carcinoma occurred in 1.4 per cent. Kirsner, Palmer, Maimon and Ricketts [11] recently described 2 cases of carcinoma in a selected group of 100 cases of ulcerative colitis. In a review of 630 cases of chronic ulcerative colitis at the Lahey Clinic during the period from 1927 to 1946, Cattell and Sachs [12] reported that 166 patients (26 per cent) were operated on; of these, 7 per cent exhibited carcinoma. The average duration of colitis in the patients with carcinoma was nine years.

For clarification of the problem of the development of carcinoma from pseudopolyposis in chronic ulcerative colitis, a definition of terms appears advisable. This is particularly true because, both in the literature and in medical practice, there is considerable confusion as to the etiology, pathology, differentiation and treatment of intestinal polyps. Any localized projection of tissue, sessile or pedunculated, may be regarded as a polyp. In the intestine the lesion generally arises from the mucosa and projects into the lumen of the bowel. It may, however,

6. Cattell, R. B.: Indications for Colectomy, S. Clin. North America **24**:656 (June) 1944.

7. Bargen, J. A., and Sauer, W. G.: The Association of Chronic Ulcerative Colitis and Carcinoma, Clinics **3**:516 (Oct.) 1944.

8. Ricketts, W. E.; Benditt, C. P., and Palmer, W. L.: Chronic Colitis with Infantilism and Carcinoma of Colon, Gastroenterology **5**:272 (Oct.) 1945.

9. Cattell, R. B., and Boehme, E. J.: Chronic Colitis Complicated by Carcinoma of Colon and Rectum, S. Clin. North America **26**:641 (June) 1946.

10. Ricketts, W. E., and Palmer, W. L.: Complications of Chronic Nonspecific Colitis, Gastroenterology **7**:55 (July) 1946.

11. Kirsner, J. B.; Palmer, W. L.; Maimon, S. N., and Ricketts, W. E.: Clinical Course of Chronic Nonspecific Ulcerative Colitis, J. A. M. A. **137**:922 (July 10) 1948.

12. Cattell, R. B., and Sachs, E., Jr.: Surgical Treatment of Ulcerative Colitis, J. A. M. A. **137**:929 (July 10) 1948.

arise in the deeper portions of the wall, grow toward the lumen and push mucosa ahead of it. Two examples are the lipomatous polyp of the submucosa and the leiomyoma of the muscularis. The polyps with which the present report is concerned are those arising from the mucosa. They are of two varieties: the inflammatory polyp and the neoplastic polyp. The former is associated with chronic ulcerative colitis, is inflammatory in origin and represents pinched-off bits of intact mucosa, between areas of geographic or linear ulceration. This is the only

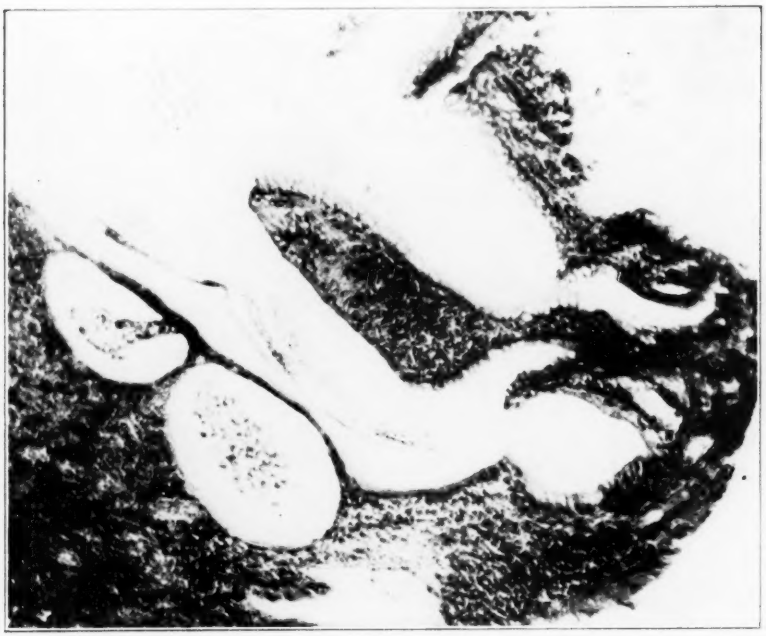

Fig. 1.—Low power photomicrograph of pseudopolyp. Note cystic glands, some lined with atrophic epithelium and others with columnar and goblet cells.

mucosa from which regeneration of epithelium can occur to cover denuded areas. These pseudopolyps vary considerably in size and shape and are usually smooth and sessile. They are almost invariably edematous, giving the appearance of lusterless, skinned grapes. Microscopically, the covering epithelium may be intact, or partly so; the underlying tissue is infiltrated with polymorphonuclear, plasma and round cells. Often the epithelium lining the crypts of Lieberkühn is distorted or displaced, so that the normal topography is destroyed. The lining cells are normal; there is no penetration of the basement membrane, and

goblet cells carry on their normal activity (fig. 1). If access of their secretion to the lumen of the bowel is prevented by closure of the mouths of the glands or ducts, cystic changes occur, with retention of mucus.

Fig. 2.—Pseudopolyps passed by rectum in a case of chronic ulcerative colitis.

Fig. 3.—Low power photomicrograph of pseudopolyp. Note distorted glands and intact solitary acuminate lymph nodule.

The epithelium may atrophy. This process, with the associated edema, gives rise to the polyps of chronic ulcerative colitis (pseudopolyposis cystica of Virchow). When the neck of the polyp is narrow or poorly

vascularized, the polyp may necrose and slough or undergo torsion and be passed with the intestinal contents (fig. 2). We have never noted active proliferation of epithelium in pseudopolyps to the point of neoplasia. We have repeatedly seen active extension of the epithelium to cover ulcerated areas, just as, if some lymphoid tissue remains, regeneration of solitary lymph nodules occurs. Indeed, not only does fresh, pearly epithelium cover the ulcerated areas during the healing phase of chronic

Fig. 4.—Pseudopolyposis in chronic ulcerative colitis. Note smooth polyps between areas of linear and geographic ulceration (Felsen, J.: Acute and Chronic Bacillary Dysentery, *Am. J. Path.* **12**:395 [May] 1936).

ulcerative colitis, but in time the pseudopolyps may flatten out, ultimately appearing as normal mucosa. We have seen this phenomenon in many patients who have repeatedly been examined for a number of years. It has been our impression that inflammatory polyposis at one time or another is a rather constant phenomenon in cases of chronic colitis with extensive ulceration. At one stage, biopsy may actually reveal intact solitary acuminate lymph nodules within a polyp (fig. 3). We have never noted gross or microscopic evidence of malignancy in polyps due

to chronic ulcerative colitis. Swinton and Warren,[13] in a study of the histopathology of a large series of intestines of patients with chronic ulcerative colitis, did not detect evidence of malignancy in any polyp. It may be of interest that the inflammatory polyposis present in the colon often extends into the ileum (figs. 4 and 5). Yet, to our knowledge, the proponents of malignancy due to pseudopolyposis have never noted such malignancy in the ileum. If their concept is correct, there is

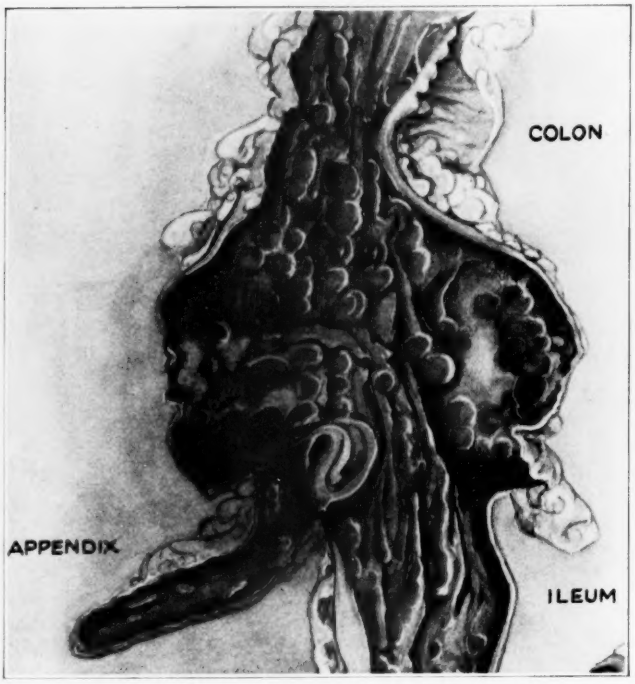

Fig. 5.—Pseudopolyposis in chronic ulcerative colitis involving colon, appendix and ileum (Felsen, J.: Bacillary Dysentery, Colitis and Enteritis, Philadelphia, W. B. Saunders Co., 1945).

no reason that the ileum should not be involved, since the pathologic condition of pseudopolyposis would be identical with that in the colon. Primary adenocarcinoma of the ileum is rare, but it does occur. We have seen at least 1 instance, in a patient without any other pathologic lesions of the intestine.

13. Swinton, N. W., and Warren, S.: Polyps of the Colon and Rectum and Their Relation to Malignancy, J. A. M. A. **113**:1927 (Nov. 25) 1939.

In an attempt to determine a basis for the occurrence of carcinoma in patients with pseudopolyposis, we have found it necessary to consider the possibility of the development of malignancy as an independent phenomenon, entirely unrelated to chronic ulcerative colitis. In considering the second type of mucosal polyp—the adenoma—we shall omit, for obvious reasons, the condition known as adenomatosis coli, in which the entire colon, and rarely the stomach and small intestine, is studded with innumerable adenomas. The intervening mucosa is normal; the condition involves a hereditary factor of the mendelian type, usually affects several members of a family and is prone to multicentric malig-

Fig. 6.—Neoplastic polyps (adenomas) in varying stages of development, from a small sessile type to pedunculated forms. Note delicate lobulation, in contrast to smooth surface of inflammatory pseudopolyp (fig. 4).

nant degeneration. It is of relatively infrequent occurrence. This is not the case, however, with widely separated adenomatous polyps, one or more of which are frequently found in the colon. In a series of 955 necropsies on persons of various ages, at the Bronx Hospital, the incidence of two or more adenomatous polyps in the colon was 6.4 per cent. When the newborn are excluded, the incidence was 9.6 per cent. These figures are for patients without ulcerative colitis. They represent a fair cross section of the population in the area in which our patients with ulcerative colitis live. It is reasonable to assume that adenomatous polyps occur in patients with chronic ulcerative colitis at a rate similar to that for patients without the disease. The incidence of carcinoma of the colon

among 12,025 patients admitted to the Bronx Hospital in 1946 and 1947 was 99, or 0.8 per cent (this figure excludes the newborn).

The growth of adenomatous polyps has been traced from small, sessile, localized areas of glandular hyperplasia, scarcely visible to the naked eye, to the large, reddish, delicately lobulated, solid masses, like mushrooms at the end of a pedicle of mucosa (figs. 6, 7 and 8). The pedicle is generally broad at the base, where it is continuous with normal mucosa, and somewhat tapering near the top, where it joins the tumor.

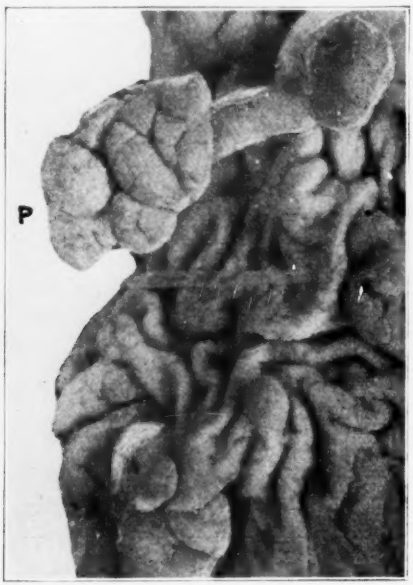

Fig. 7.—Adenoma (*P*) with long pedicle, at the base of which is a sessile adenoma.

These pedicles, at least the longer ones, merely represent normal mucosa, which has been drawn away from its loose attachment to the submucosa when the intestine attempted to rid itself of the tumor, as it would a foreign body. In some instances traction on the mucosa by the dead weight of the tumor appears to have been responsible for formation of the pedicle. The latter may carry with it some submucosa, and occasionally the muscularis and serosa as well (fig. 9). When the serosa is drawn up into the base of the pedicle, there is danger of opening the peritoneal cavity in snaring the polyp.

It is rather generally accepted that adenomatous polyps form the basis for many carcinomas of the large bowel. This does not imply that all adenomas tend to become malignant. When malignancy supervenes, a previously pedunculated tumor tends to become sessile and to grow, both toward the lumen of the bowel and intramurally to the submucosal lymphatic plexus, which may act as a formidable barrier for some time. Eventually the neoplastic process breaks through to involve the lymphatics of the inner (circular) muscularis, the intermuscular lymphatics, those of the outer (longitudinal) muscularis and, finally, the serosa and

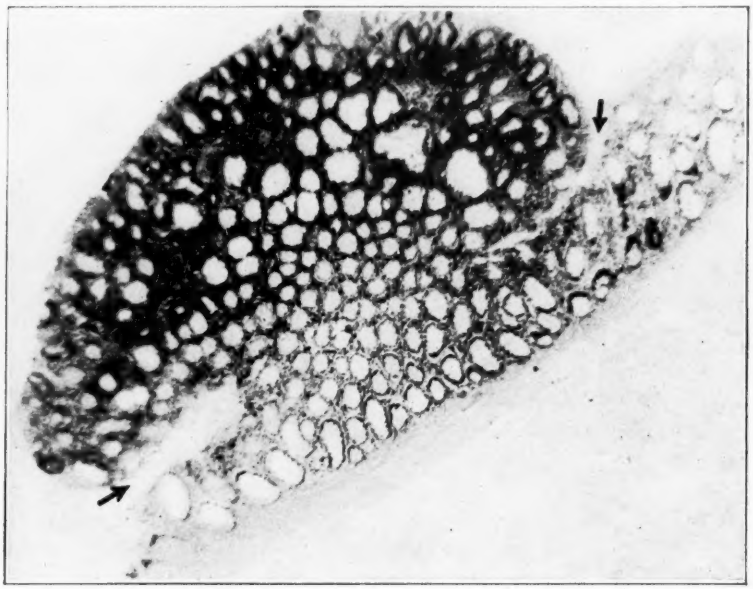

Fig. 8.—Low power photomicrograph of small pedunculated adenoma. Arrows indicate short pedicle.

extraserosal lymph nodes (fig. 9). The neoplastic glands are disposed in the general direction of the involved lymphatics (circular or longitudinal). Intramural spread is fan shaped, so that a relatively small malignant adenoma or adenoma destruens on the mucosal surface appears as a much larger tumor on the serosal aspect.

Pseudopolyposis is inflammatory in origin and associated with active infection, as evidenced by ulceration and intramural cellular infiltration. Adenomatous polyps exhibit none of these characteristics. No acceptable

evidence has been presented with respect to their origin. Vague statements regarding "chronic irritation" and infection have often been presented, but all that is really known at present is that adenomatous polyps represent an autonomous new growth of tissue. The pseudopolyposis of chronic ulcerative colitis is merely a polypoid form of mucosa which has survived a process of necrosis associated with inflammation. Our studies indicate that sufficient active proliferation of epithelium

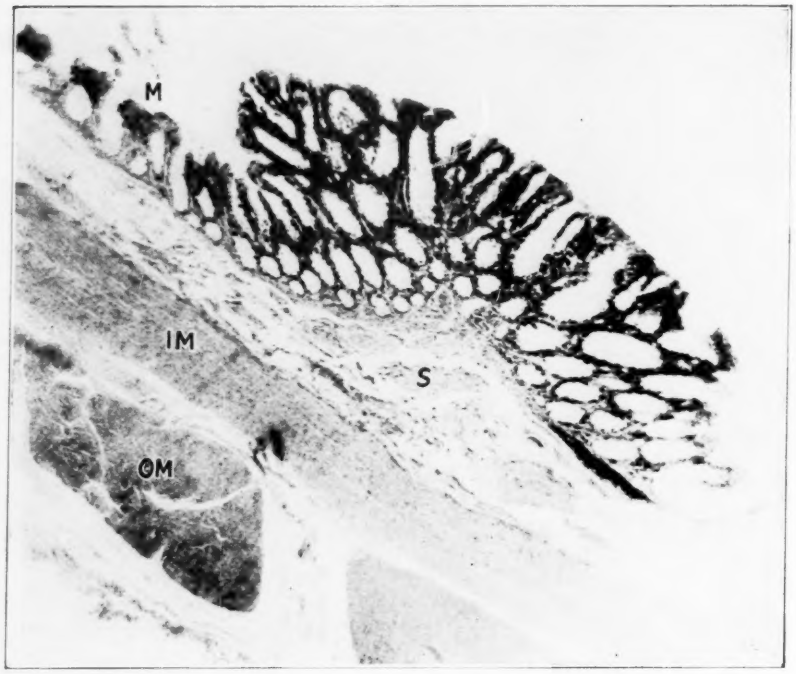

Fig. 9.—Photograph of small sessile adenoma (higher power than figure 8). Some submucosa (*S*) is being drawn up into the base. *M* indicates mucosa; *I M*, inner (circular) muscularis; *O M*, outer (longitudinal) muscularis.

occurs during the healing phase to cover adjacent denuded areas, but in our experience the process has never progressed to a stage that could be interpreted as neoplasia. The end result is a smooth, flat mucosa, not a tumor. We have occasionally noted one or more adenomas in cases of chronic ulcerative colitis. The incidence, however, is well below that in our control group referred to previously.

CLINICAL DATA

A statistical analysis of 855 cases of ulcerative colitis follows. All patients were examined repeatedly over considerable periods; 134 (15.7 per cent) exhibited polyposis. In the published reports on the development of carcinoma in polyposis, two striking features appear: One is the development of a malignant growth in young persons with polyposis; the other is the frequent development of a malignant growth in those

TABLE 1.—*Distribution of Polyposis According to Age in 134 Cases*

Age, Years	Number of Cases	Percentage
0-9	2	1.0
10-19	7	6.0
20-29	34	25.0
30-39	35	26.0
40-49	35	26.0
50-59	16	12.0
60-69	5	4.0

TABLE 2.—*Distribution of Polyposis According to Duration of the Disease in 134 Cases*

Duration, Years	Number of Cases	Percentage
1-4	60	44.8
5-26	74	55.2

TABLE 3.—*Duration of Polyposis According to Selected Age Groups (98 Cases)*

	Number of Cases of Polyposis	
Age, Years	Five Years or More	Nine Years or More
20-29	21	8
30-39	16	11
40-49	23	11
50-59	0	8
Totals	60	38

patients who have had chronic ulcerative colitis for a long time (five years or more and nine years or more, in different studies). We have therefore analyzed our figures from the standpoint of these two factors.

The youngest patient was 20 months old and the oldest 67 years. Fifty per cent of patients were in the 20 to 39 year age groups and 42 per cent in the 40 to 69 year age groups.

Seventy-four patients (55.2 per cent) had had the disease five years or longer, and 38 patients (28.3 per cent), nine years or longer. The extremes of duration in the series of 134 patients were two months and twenty-six years.

None of the 134 patients with polyposis exhibited a malignant tumor in spite of a fairly even distribution, both as to age groups and long duration. None of the entire group of 855 patients with chronic ulcerative colitis has shown evidence of a malignant growth at the time of this report, although the majority have had the disease for many years and have been repeatedly examined during this period. It is reasonable to assume that even had we missed a diagnosis of malignant growth initially, the subsequent follow-up examinations would have revealed our error.

When we consider the relatively high figures for the incidence of carcinoma in cases of chronic ulcerative colitis published by some authors, it is evident that the problem is a serious one. Such data might be used to justify excision of the colon in all long-standing cases of the disease, as a prophylactic procedure against the development of a malignant process. In our opinion this would involve much needless surgery, and possibly loss of life, and a permanent artificial stoma would be necessary. On the basis of the facts presented, it is difficult to accept without question the direct relation of pseudopolyposis and chronic ulcerative colitis to carcinoma. On the contrary, our own observations indicate that carcinoma, when it does develop in a case of pseudopolyposis with chronic ulcerative colitis, probably occurs as an entirely independent phenomenon, possibly on the basis of a preexisting adenoma. We have never noted the development of a true neoplastic adenomatous polyp from an inflammatory pseudopolyp. Further support of the lack of relation between carcinoma and pseudopolyposis is offered by control studies in cases of carcinoma without chronic ulcerative colitis.

SUMMARY

A series of 855 cases with chronic ulcerative colitis, including 134 with pseudopolyposis, is presented. Clinical and pathologic studies failed to reveal a single case of carcinoma. It is suggested that the latter may occur as an entirely independent phenomenon, possibly on the basis of a preexisting adenoma.

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SURVIVAL AFTER RECENT MYOCARDIAL INFARCTION

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RECENTLY we have analyzed the factors concerned with the immediate prognosis in recent myocardial infarction.[1] In this report we wish to present the results of our analysis on the long term prognosis. Of the 572 cases previously reported, 507 were selected for this study. These patients were the ones seen in the hospital during the period from 1940 to 1945, inclusive. They represent 0.48 per cent of the total admissions for these years. The selection of these cases was based on the electrocardiographic findings, correlated with the clinical data and, when available, with the necropsy observations. Considerable reliance was placed on unmistakable signs of recent myocardial infarction in the electrocardiogram. The follow-up observations on these patients were made through private physicians, the hospital outpatient department or direct correspondence with the patients known to be alive. Seventeen of the 507 patients could not be followed. A number of the patients had died by the time of the follow-up study, which was made in January 1947. It was possible to obtain complete follow-up data, including electrocardiograms, on 100 of these patients. Our findings in the latter group will be the subject of another communication.[2] Information as to the status of patients who could not

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1. Minta, S. S., and Katz, L. N.: Recent Myocardial Infarction: An Analysis of Five Hundred and Seventy-Two Cases, Arch. Int. Med. **80**:205 (Aug.) 1947.

2. Mills, G. Y.; Cisneros, F., and Katz, L. N.: Observations on One Hundred Patients with Myocardial Infarction Who Survived Up to Six Years, Arch. Int Med. to be published.

be contacted for personal interviews was obtained from their private physicians or from the records of the outpatient department. In the case of the patients who died in the interim, an effort was made to determine as closely as possible the data on and the circumstances concerned with their death. This information was obtained from the private physician's records, from members of the family or, in some instances, from the hospital record obtained on a subsequent terminal

TABLE 1.—*Mortality and Survival Rate of 507 Patients with Recent Myocardial Infarction Occurring from 1940 to 1945; Followed for Various Periods Up to More Than Six Years.**

1	2	3	4	5	6	7	8	9
Period, Months	Total in Group, No.	Total Known Deaths, No.	Death Rate, per Cent	Unable to Trace After Period Indicated, No.	Followed Only for Months Indicated and Known to Be Alive, No.	Total Followed and Condition Known, No.	Known to Be Alive at End of Period	
							No.	per Cent
First 2	488	135	27.6	81	..	488	353	72.3
2-6	272	22	8.1	7	..	407	250	61.4
6-12	243	23	9.5	11	24	400	220	55.0
12-24	185	15	8.1	11	40	365	170	46.6
24-36	119	13	10.9	7	32	314	106	33.7
36-48	67	3	4.5	2	14	275	64	23.3
48-60	48	6	12.5	3	17	259	42	16.2
60-72	22	0	0	1	17	239	22	9.2
More than 72	4	0	0	0	0	221	4	....
Cumulative totals for deaths	488	217	81.2					

* We were unable to trace 19 patients, and do not know their span of life.

admission. Thus, we were able to obtain a complete follow-up study on 19 per cent of the patients; 3 per cent could not be traced, and some information was obtained on the remaining 78 per cent, of whom 59 per cent were known to be dead and 41 per cent were alive at the time of the follow-up study.

RESULTS

Mortality and Survival Rate.—The first problem considered was the relation of survival and mortality rates at various periods after the occurrence of the infarct. These data are assembled in table 1. It will be seen that of the 488 patients followed, 217, or 44.6 per cent, had died. The mortality rate was greatest in the first two months, being

27.6 per cent. This is higher than the 8 per cent reported by Master and his associates,[3] the 15 per cent reported by Drake [4] or the 16.2 per cent reported by Connor and Holt,[5] but is of the order reported by Howard.[6] The rate after the first two months lessened progressively.[7] It will be seen that the greatest mortality rate occurred in the first year and was less, and more or less steady, during the second to the fifth year. The cumulative mortality rate illustrated in figure 1 shows that by the end of the fifth and sixth years, 81 per cent of the patients would be dead, and only 19 per cent would survive a period of five to six years. Obviously, the totals in the group followed after the

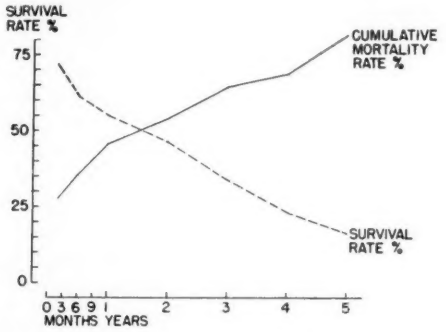

Fig. 1.—Cumulative mortality rate and survival rate at various periods after myocardial infarction (table 1).

3. Master, A. M.; Jaffe, H. L., and Dack, S.: Treatment and Immediate Prognosis of Coronary Artery Thrombosis (Two Hundred and Sixty-Seven Attacks), Am. Heart J. **12**:549, 1936.

4. Drake, E. H.: Long Survival Following Coronary Thrombosis, Am. Heart J. **20**:634, 1940.

5. Connor, L. A., and Holt, E.: The Subsequent Course and Prognosis in Coronary Thrombosis (An Analysis of Two Hundred and Eighty-Seven Cases), Am. Heart J. **5**:705, 1930.

6. Howard, T.: Coronary Occlusion, Based on the Study of One Hundred and Sixty-Five Cases, M. Times & Long Island M. J. **62**:337, 1934.

7. To obtain the mortality rate for the later intervals given in column 4, we first obtained the total in the group observed in the periods concerned (shown in column 2). This was done by subtracting from the total of the previous period (in column 2) the sum of the known dead in that period (in column 3) plus those unable to be traced after that period (in column 5) and those who were followed only for the period indicated (in column 6) because the follow-up was not extended beyond January 1947.

fifth year are too small to be considered quantitative in any sense. That this estimate of survival time is correct is shown by another calculation, given in columns 7, 8 and 9 of table 1. Here are presented the number and percentage of patients known to be alive at the end of each period. The percentage survival is also presented in figure 1. It was found that 72 per cent of the patients survived the first two months after infarction; by the end of the year the survival rate was 55 per cent, and by the end of the five years it was only 16 per cent. Our data on survival rate at the end of five years are lower than those reported by Connor and Holt [5] and Levine and Rosenbaum [8] on smaller series.

It appears from our observation that roughly one fourth of the patients having a recent myocardial infarction would be dead at the end of two months. About one half would be dead at the end of the year, about two thirds at the end of the third year and about four fifths at the end of five years. This surprisingly high mortality rate makes the long term prognosis of a recent myocardial infarction much more serious than has been anticipated generally.

Cause of Death After First Two Months Following Recent Myocardial Infarction.—In this series, 82 patients are known to have died after the first two months following recent myocardial infarction. In 30 the cause of death was unknown. Of the remaining 52, 10 died of heart failure, 3 of pulmonary embolism, 34 of a new myocardial infarct and 5 of miscellaneous causes. In this series, there were apparently no deaths after the first two months from cerebral apoplexy or renal insufficiency. The diagnosis of the cause of death was based on the evaluation of the clinical findings, and when necropsy was obtained, on the autopsy findings. The data are summarized in table 2 and presented diagrammatically in figure 2. It is significant that 65 per cent of the patients who died after the first two months following recent myocardial infarction did so because of a new myocardial infarct. This is a higher rate than the 40 per cent reported by Levine and Rosenbaum.[8] Heart failure was a less common cause, accounting for 19 per cent; this is almost identical with the rate reported by Levine and Rosenbaum.[8] Pulmonary embolism was responsible for almost 6 per cent.

The fatal new myocardial infarct occurred most commonly in the first year after the infarction, but instances occurred in every year up to five years. More significant is the fact that all the pulmonary

8. Levine, S. A., and Rosenbaum, F. F.: Prognostic Value of Various Clinical and Electrocardiographic Features of Acute Myocardial Infarction: Ultimate Prognosis, Arch. Int. Med. **68**:1215 (Dec.) 1941.

emboli that were fatal occurred in the first year. On the other hand, the deaths due to heart failure were distributed more evenly over the five year period. One can conclude, therefore, that the hazard of pulmonary embolism is remote after the first year following infarction,

TABLE 2.—*Causes of Death of the 82 Patients Who Succumbed After First Two Months Following Recent Myocardial Infarction**

Period of Survival, Months	Heart Failure	Pulmonary Emboli	New Myocardial Infarct	Miscellaneous	Unknown	Total
2-6	1	2	11	2	6	22
6-12	2	1	8	1	11	23
12-24	3	0	5	1	6	15
24-36	2	0	5	1	5	13
36-48	1	0	2	0	0	3
48-60	1	0	3	0	2	6
60-84	0	0	0	0	0	0
Totals	10	3	34	5	30	82
Per cent of total deaths	12.2	3.7	41.4	6.1	36.6	
Per cent of deaths of known cause..	19.2	5.8	65.4	9.6		

* The diagnoses of cause of death are based principally on findings at necropsy, and when no postmortem examination was made, on clinical judgment. There were apparently no deaths due to cerebral apoplexy or renal insufficiency.

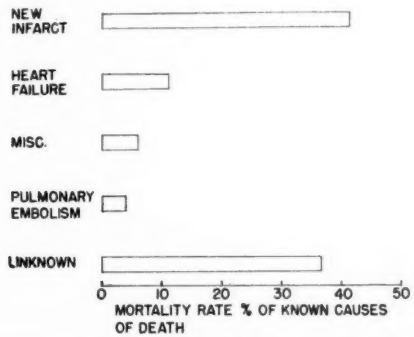

Fig. 2.—Frequency of known causes of death two months after recent myocardial infarction (table 2).

that heart failure will be the terminal event at any time during the first five years and that the most significant cause of death, recurrent myocardial infarction, may also occur at any time in the five year period, but most frequently in the first year after the original infarction.

Effect of Various Factors on Long Term Mortality Rate of Recent Myocardial Infarction.—In table 3 and in figure 3 are summarized our

TABLE 3.—*Effect of Various Factors on the Long Term Mortality Rate for Recent Myocardial Infarction Based on an Analysis of 507 Cases Occurring Between 1940 and 1945*

Factors	Total Cases, No.	Total Cases in Follow-up Study, No.	Total Deaths in First 2 Months		Total Deaths in Entire Period		Total Deaths After Second Month		Average Duration of Life of Those Who Died After 2 Mo., Months	Alive But Could Not Be Contacted, No.
			No.	Per Cent of Total No. of Cases	No.	Per Cent of Total No. of Cases	No.	Per Cent of Total No. of Cases	Average Duration of Life of Those Known to Have Died, Months	
Known hypertension before and at admission	256	194	71	27.7	127	49.6	56	21.9	8.8	15.5	22
Known angina pectoris up to 1 mo. prior to, or at admission	171	124	37	21.6	69	40.3	32	18.7	9.0	16.8	20
Clinical heart failure at admission	127	108	61	48.0	91	71.6	30	23.6	7.1	14.5	6
Known diabetes mellitus before or at admission	63	57	32	50.8	43	68.3	11	17.5	2.9	7.1	4
Electrocardiogram showing low voltage, ectopic rhythms, block and/or sinus tachycardia on admission	212	163	77	36.3	105	49.5	28	13.2	6.7	13.0	14
Electrocardiogram showing normal voltage, rhythms of sinus origin (exclusive of tachycardia) and no ectopic beats or block on admission	295	215	57	19.3	107	36.2	50	16.9	10.3	21.5	37
Patient asymptomatic on admission	88	55	19	21.5	25	28.4	6	6.9	12.4	44.3	14
Total group	507	488	135	26.6%	217	42.8%	82	16.2%	8.2 mo.	17.8 mo.	117

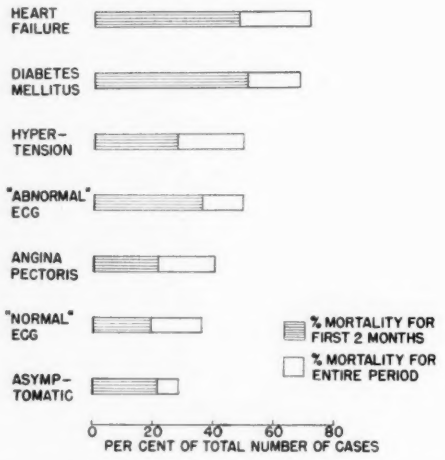

Fig. 3.—Effect of various factors on mortality rate (table 3).

experiences with several factors which might influence the long term mortality rate of recent myocardial infarction. We analyzed the effect of the following factors: (1) the presence of known hypertension (150 systolic and 90 diastolic, or over) before or at admission; (2) the presence of known angina pectoris at the time of admission and up to a month prior to admission; (3) the influence of clinical heart failure on admission; (4) the effect of known diabetes mellitus present before or on admission; (5) the influence of a cardiac status reflected by certain electrocardiographic abnormalities, such as low voltage, ectopic rhythms, heart block and/or sinus tachycardia present in the electrocardiogram on admission; (6) the influence of a cardiac status reflected by an electrocardiogram obtained on admission with normal voltage, rhythm of sinus origin (exclusive of tachycardia) and not showing block or ectopic beats, and (7) the significance of the lack of symptoms pointing to recent myocardial infarction on admission.

In order to make comparisons possible, the figures for the entire group of 507 patients are listed at the bottom of table 3. It was found that 26.6 per cent of all the patients died in the first two months and that 42.8 per cent died during the total period of observation, so that 16.2 per cent of the entire group died after the second month. The total duration of life of the known dead of the entire group averaged 8.2 months and the total duration of life of those who died after the second month was 17.8 months. These figures for duration of life are lower than those reported by others.[8]

Hypertension: By comparison with the entire group, it will be seen that hypertension had no effect on the mortality rate in the first two months,[9] but had a slight deleterious influence on the later mortality (the rate being 49.6 per cent for the group with hypertension as against 42.8 per cent for the entire group, and the rate after the second month being 21.9 per cent as against 16.2 per cent for the entire group). Furthermore, in the group with hypertension the duration of life of those who died after two months was shortened slightly (14.5 months as compared with 17.8 months for the entire group). Our results indicate therefore that while hypertension has no effect on immediate mortality in the first two months, a finding in agreement with previous observations,[9] it seems to decrease the long term survival slightly. This

9. (*a*) Mintz and Katz.[1] (*b*) Gross, H., and Engelberg, H.: Essential Hypertension: A Comparison of the Hypertensive and Non-Hypertensive Phase Following Coronary Thrombosis, Am. J. M. Sc. **199**:621, 1940.

last finding is in accord with some previous reports,[10] but others [11] indicated no such effect.

Angina Pectoris: The presence of angina pectoris had no deleterious effect on the immediate mortality in the first two months (in agreement with our previous observations [1] or on the long term mortality rate, although the average duration of life of those who died after two months was slightly shortened.

Heart Failure: The presence of heart failure on admission not only sharply increased the mortality rate in the first two months, as has been noted previously [12] (the mortality rate being 48 per cent as compared with 26.8 per cent for the entire group), but also increased the over-all mortality rate (71.6 per cent as compared with 42.8 per cent) and the mortality rate after the second month (23.6 per cent compared with 16.2 per cent). Heart failure, furthermore, significantly shortened the duration of life of those who died after the second month (14.5 months as compared with 17.8 months). Thus, it is apparent that heart failure strikingly worsens the prognosis, both immediately and over the five year period. This has been reported previously.[13]

Diabetes Mellitus: Diabetes, as previously found,[14] strikingly increased the mortality rate in the first two months (50.8 per cent as

10. (*a*) Master, A. M.; Dack, S., and Jaffe, H. L.: Coronary Thrombosis: Investigation of Heart Failure and Other Factors in Its Course and Prognosis, Am. Heart J. **13**:330, 1937. (*b*) Rosenbaum, F. F., and Levine, S. A.: Prognostic Value of Various Clinical and Electrocardiographic Features of Acute Myocardial Infarction: I. Immediate Prognosis, Arch. Int. Med. **68**:913 (Nov.) 1941.

11. (*a*) Levine and Rosenbaum.[8] (*b*) Vander Veer, J. B., and Brown, L. E.: Diagnosis and Prognosis of Coronary Occlusion; Electrocardiogram As Aid, Pennsylvania M. J. **39**:303, 1936. (*c*) Bedford, D. E.: Prognosis in Coronary Thrombosis, Lancet **1**:223, 1935. (*d*) Chambers, W. N.: Blood Pressure Studies in One Hundred Cases of Coronary Occlusion with Myocardial Infarction, Am. J. M. Sc. **213**:40, 1947. (*e*) Bland, E. F., and White, P. D.: Coronary Thrombosis (with Myocardial Infarction): Ten Years Later, J. A. M. A. **117**:1171 (Oct. 4) 1941. (*f*) Gross and Engelberg.[9b]

12. Mintz and Katz.[1] Rosenbaum and Levine.[10b]

13. Levine and Rosenbaum.[8] Rosenbaum and Levine.[10b]

14. (*a*) Mintz and Katz.[1] (*b*) Gross and Engelberg.[9b] (*c*) Root, H. F., and Sharkey, T. P.: Coronary Arteriosclerosis in Diabetes Mellitus, New England J. Med. **215**:605, 1936. (*d*) Root, H. F.; Bland, E. F.; Gordon, W. H., and White, P. D.: Coronary Atherosclerosis in Diabetes Mellitus: A Post Mortem Study, J. A. M. A. **113**:27 (July 1) 1939. (*e*) Rabinowitch, I. M.: Arteriosclerosis in Diabetes: Effects of High Carbohydrate-Low Calorie Diet, Ann. Int. Med. **8**:1436, 1935. (*f*) Blotner, H.: Coronary Disease in Diabetes Mellitus, New England J. Med. **203**:709, 1930. (*g*) Enklewitz, M.: Diabetes and Coronary Thrombosis: Analysis of Cases Which Came to Necropsy, Am. Heart J. **9**:386, 1934.

compared with 26.6 per cent) and also the over-all mortality rate (68.3 per cent as compared with 42.8 per cent). However, the long term mortality rate was not greatly altered, the mortality rate after the first two months being 17.5 per cent as against 16.2 per cent for the whole group. But the average duration of life for the patients who died after two months was greatly shortened (7.1 months as compared with 17.8 months). Apparently, the presence of diabetes, while not increasing the mortality rate after two months, led to earlier death among those that did die. It is also significant that diabetes sharply reduced the duration of life of the known dead over the entire period of study even more strikingly (2.9 months as compared with 8.2 months), suggesting that even in the patients who died in the first two months the ill effects occurred sooner than in the whole group. We may conclude therefore that, by and large, the ill effects of diabetes so far as death is concerned manifest themselves early in the period after infarction and that the later prognosis is no worse than for the group as a whole. Therefore, a diabetic patient who survives the first six or eight months after the infarction has no worse a prognosis than the nondiabetic patient.

Certain Electrocardiographic Abnormalities: The influence of certain abnormalities in the electrocardiogram listed in the fifth line of table 3 was definitely to increase the mortality rate in the first two months (36.3 per cent as compared with 26.6 per cent). This is in accord with the observations previously reported by us [1] except that we had not previously analyzed the data for the factor of low voltage. The ill effects of auriculoventricular block,[15] intraventricular block [16] and low voltage [17] were noted previously, but other authors [10b] considered low voltage a favorable sign. In this group the mortality rate after the first two months was not significantly different than that for the whole group, so that the mortality rate for the entire period was influenced only by the greater mortality in the first two months. Apparently, however, the average duration of life was shortened both for all

15. (*a*) White, P. D., and Bland, E. F.: A Further Report on the Prognosis of Angina Pectoris and of Coronary Thrombosis: A Study of Five Hundred Cases of the Former Condition and of Two Hundred Cases of the Latter, Am. Heart J. **7**:1, 1931. (*b*) Stone, C. T.: Future of Patient with Coronary Occlusion, New Orleans M. & S. J. **95**:305, 1943.

16. (*a*) White and Bland.[15a] (*b*) White, P. D.: The Prognosis of Angina Pectoris and of Coronary Thrombosis, J. A. M. A. **87**:1525 (Nov. 6) 1926. (*c*) Stone.[15b]

17. Barnes, A. R.: Electrocardiogram in Myocardial Infarction: Review of One Hundred and Seven Clinical Cases and One Hundred and Eight Cases Proved at Necrospy, Arch. Int. Med. **55**:457 (March) 1935.

those who died during the period of study and for those who died after two months (6.7 months as compared with 8.2 months and 12 months as compared with 17.8 months). All electrocardiographic abnormalities have been considered to be of poor prognostic significance at one time or another,[18] especially when more than one of them occurs simultaneously.[19] Levine,[20] however, suggested that auricular fibrillation has no influence on prognosis. We may conclude, therefore, from our data that the presence of low voltage, ectopic rhythms, heart block and/or sinus tachycardia on admission has no effect on the mortality rate after the first two months, but definitely increases the mortality rates for the first two months. Thus, those patients in this group who survive the first six or eight months have as good a prognosis as the whole group.

Electrocardiograms Without Low Voltage or the Aforementioned Abnormalities: Patients with electrocardiograms which on admission failed to show low voltage or the abnormal rhythms considered in the preceding paragraph showed a much better prognosis as regards the immediate mortality rate (19.3 per cent as compared with 26.6 per cent), but their mortality rate after the first two months was no better than that for the group as a whole (16.9 per cent as compared with 16.2 per cent). Conner and Holt,[5] however, indicated that patients with normal rhythm and voltage had a better long term prognosis. The better over-all prognosis in terms of mortality rate is due, therefore, to the more optimistic outlook in the first two months. This also explains why the over-all duration of life for those who died in this group was

18. (*a*) Rosenbaum and Levine.[10b] (*b*) Master, A. M.; Dack, S., and Jaffe, H. L.: Disturbances of Rate and Rhythm in Acute Coronary Thrombosis, Ann. Int. Med. **11**:735, 1937. (*c*) Partial and Complete Heart Block in Acute Coronary Occlusion, Am. J. M. Sc. **196**:513, 1938; (*d*) Age, Sex and Hypertension in Myocardial Infarction, Due to Coronary Occlusion, Arch. Int. Med. **64**:767 (Oct.) 1939. (*e*) Salcedo-Salgar, J., and White, P. D.: Relationship of Heart Block, Auriculoventricular and Intraventricular, to Clinical Manifestations of Coronary Disease, Angina Pectoris, and Coronary Thrombosis, Am. Heart J. **10**:1067, 1935. (*f*) Levine, S. A.: Coronary Thrombosis: Its Various Clinical Features, Medicine **8**:245, 1929. (*g*) Willius, F. A., and Killins, W. A.: The Occurrence and Significance of the Electrocardiograms of Low Voltage, Arch. Int. Med. **40**:332 (Sept.) 1927. (*h*) Master, A. M.; Dack, S., and Jaffe, H. L.: Bundle Branch Block in Acute Coronary Artery Occlusion, Am. Heart J. **16**:283, 1938. (*i*) Woods, R. M., and Barnes, A. R.: Factors Influencing Immediate Mortality After Coronary Occlusion, ibid. **24**:4, 1942.

19. Ken, W. J.: The Present Status of Electrocardiography in the Diagnosis, Prognosis and Treatment of Heart Disease, California & West. Med. **23**:417, 1925.

20. Levine, S. A.: Coronary Thrombosis: Its Various Clinical Features, Medicine Monographs, Baltimore, Williams & Wilkins Company, 1929, vol. 16.

slightly longer than that for the entire group (10.3 months as compared with 8.2 months). It may be concluded, therefore, that while the absence of low voltage and sinus tachycardia, heart block and ectopic rhythms improves the immediate mortality, this seems to have no influence on the long term prognosis. Such patients who survive after the second month appear to have the same outlook for survival as the group as a whole.

Absence of Symptoms: The situation is quite different for patients with recent myocardial infarction who were free from symptoms on admission. The immediate mortality was little different from that for

TABLE 4.—*Influence of Age and Sex on Long Term Mortality Rate of Recent Myocardial Infarction as Revealed by an Analysis of 507 Cases Occurring Between 1940 and 1945*

Age and Sex in Years	Total No. Cases	Total No. Cases in Follow-up Study	Total No. Deaths	Total Deaths First 2 Months No.	Total Deaths After 2 Months No.	Average Duration of Life of Those Who Died, Mo.	Average Duration of Life of Those Who Died After 2 Mo., Months
Male	341 (67%)	328	135 (39.6%)	76 (22.3%)	59 (17.3%)	9.2	18.4
Female	166 (33%)	160	82 (49.4%)	59 (35.5%)	23 (13.9%)	6.2	17.0
31-40	21	20	4 (19.1%)	2 (9.5%)	2 (9.5%)	9.0	17.7
41-50	88	83	23 (26.1%)	15 (17.0%)	8 (9.1%)	7.6	17.2
51-60	174	166	73 (42.0%)	40 (22.9%)	33 (18.9%)	10.0	19.9
61-70	173	171	89 (52.0%)	59 (34.1%)	30 (17.3%)	9.1	20.8
71 and above	51	48	28 (54.9%)	19 (36.3%)	9 (17.6%)	5.1	13.3
Total group	507	488	217 (42.8%)	135 (26.6%)	82 (16.2%)	8.2	17.8

the entire group, but the long term mortality was strikingly better (6.9 per cent as compared with 16.2 per cent), making the over-all mortality rate less (28.4 per cent as compared with 42.8 per cent). In addition, it is quite clear that the average duration of life of those who did die was considerably prolonged (44.3 months as compared with 17.8 months and 12.4 months as compared with 8.2 months respectively). Thus, it may be concluded that the absence of symptoms at the time of infarction offers a better ultimate prognostic outlook but does not alter the immediate prognosis in the first two months.

Conclusion: This analysis of the influence of various factors on the long term prognosis, as well as on the immediate prognosis, has shown the significance of certain factors on prognosis. Such an analysis should, if verified in further studies, give the clinician important clues whereby he can judge factors influencing prognosis in cases of recent myocardial infarction.

Effects of Age and Sex on Long Term Mortality.—In table 4 and figure 4 are summarized our data showing the influence of age, according to decades, and sex on the mortality during the first two months following infarction and also the mortality rate after two months. It is obvious that mortality rate for the first two months, the mortality rate for the entire period and the mortality rate after two months tended to increase as the patient's age increased. Apparently, the older patients were more adversely affected by infarction even when they survived the first two months than were the younger patients. Myocardial infarction, therefore, is a much more serious circumstance in the

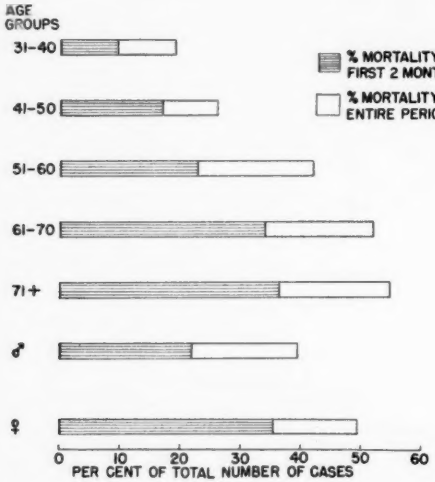

Fig. 4.—Influence of age and sex on mortality rate (table 4).

old than in the young. This is in accord with the findings reported by other investigators.[21]

21. (*a*) Master, Jaffe and Dack.[3] (*b*) Connor and Holt.[5] (*c*) Levine and Rosenbaum.[8] (*d*) White and Bland.[15] (*e*) King, H. C.: Prognosis in Coronary Heart Disease After Coronary Occlusion, Ohio State M. J. **33**:524, 1937. (*f*) Cooksey, W. B.: Coronary Thrombosis: Follow-Up Studies with Especial Reference to Prognosis, J. A. M. A. **104**:2063 (June 2) 1935. (*g*) Glendy, R. E.: Levine, S. A., and White, P. D.: Coronary Disease in Youth: Comparison of One Hundred Patients Under Forty with Three Hundred Persons Past Eighty, ibid. **109**:1775 (Nov. 27) 1937. (*h*) Master, A. M., and Dack, S.: Rehabilitation Following Acute Coronary Artery Occlusion, ibid. **115**:828 (Sept. 7) 1940. (*i*) Rathe, H. W.: Myocardial Infarction: Clinical Features and Prognosis, ibid.

(*Footnote continued on next page*)

Sex, too, plays a definite role in determining the mortality rate. The immediate mortality was greater in women than in men, but after the first two months the mortality rate was slightly less for women than for men. Rosenbaum and Levine [10b] reported a slightly greater mortality for women in the immediate phase and a longer life for men ultimately. The higher mortality rate in the first two months is responsible for the fact that the mortality rate for the entire period was higher for women than for men in our series. As pointed out previously,[1] the higher immediate mortality rate in women is due to the fact that infarction occurs in women at an older age and the percentage of diabetic patients among them is higher.

Effect of the Location of the Infarct on the Mortality Rate.—The data on this factor are summarized in table 5. In confirmation of

TABLE 5.—*Relation Between Location of Infarct and Mortality Both Immediate and After the Second Month and the Total Number of Deaths*

Location of Infarct	Total Number	Mortality First 2 Months		Mortality After Second Month		Total Deaths	
		Number	Per Cent	Number	Per Cent	Number	Per Cent
Anterior	220	57	25.9	36	16.4	93	42.2
Posterior	173	49	28.3	27	15.7	76	43.9
Lateral *	48	13	27.1	3	6.3	16	33.3
Atypical	66	16	24.2	16	24.2	32	48.4
Totals	507	135	26.6	82	16.2	217	42.8

* Anterolateral, posterolateral and lateral.

our previous report,[1] the mortality rate during the first two months was little affected by the location of the infarct. However, the mortality rate after the first two months was definitely less for the infarcts of the lateral wall than for those of the anterior or posterior wall. There

120:90 (Sept. 12) 1942. (*j*) Hedley, O. F.: Five Years' Experience (1933-37) with Mortality from Acute Coronary Occlusion in Philadelphia, Ann. Int. Med. **13**:598, 1939. (*k*) Wilhelmy, E. W., and Helwig, F. C.: Clinical and Pathologic Studies of Coronary Disease: Analysis of Eighty-Eight Cases, J. Missouri M. A. **32**:476, 1935. (*l*) Applebaum, E., and Nicolson, G. H. B.: Occlusive Diseases of Coronary Arteries: An Analysis of the Pathological Anatomy in One Hundred and Sixty-Eight Cases with Electrocardiographic Correlation in Thirty-Six of These, Am. Heart J. **10**:662, 1935. (*m*) Mullins, W. L.: Age Incidence and Mortality in Coronary Occlusion: Review of Four Hundred Cases, Pennsylvania M. J. **39**: 332, 1936. (*n*) Parkinson, J., and Bedford, D. E.: Cardiac Infarction (Coronary Thrombosis), Lancet **1**:4, 1928. (*o*) Bean, W. B.: Infarction of the Heart: Morphological and Clinical Appraisal of Three Hundred Cases; Predisposing and Precipitating Conditions, Am. Heart J. **14**:684, 1937.

was no difference in the mortality rate after the first two months between infarcts of the anterior and those of the posterior wall. However, in cases in which the electrocardiographic pattern was classified as atypical, the mortality rate was greater than for the whole group. While we have no explanation for the better long term outlook in cases of infarct of the lateral wall, there are several possible explanations for the poorer outlook in cases of infarcts with atypical electrocardiographic appearance. An atypical electrocardiographic appearance in a case of myocardial infarct is more apt to occur when the infarct is not the first or when the infarct complicates advanced coronary disease or other involvement of the heart. Both these circumstances would tend to make the survival time of the patient shorter and add significantly to the gravity of the postinfarction period. The criteria used in locating the infarct are those used in this department.[22]

SUMMARY AND CONCLUSIONS

The results of an analysis of 507 cases of recent myocardial infarction are presented. The purpose of this study was to determine the factors concerned in long term prognosis.

It was found that the mortality rate was greatest in the first two months and lessened progressively. The mortality rate continued to be high for the first year and then remained fairly steady from the second to the fifth year. By the end of the fifth to the sixth year, 81 per cent of the patients were dead. About one fourth of the patients died in the first two months, about one half had died at the end of a year, about two thirds at the end of the third year and approximately four fifths at the end of five years. Thus, the survival rate varied from 72 per cent for the first two months and 55 per cent for the first year to 16 per cent for five years.

Of the 52 patients who died after the second month following infarction in which the cause of death was known, 19 per cent died of heart failure, 6 per cent of pulmonary embolism, 65 per cent of a new myocardial infarct and 10 per cent of miscellaneous causes. There were no deaths after the first two months from cerebral apoplexy or renal insufficiency. We conclude, therefore, that a new infarct is hazardous, and, while it may occur at any time during the five year period, it is most frequent in the first year of the illness.

Hypertension on admission had no effect on the mortality rate in the first two months but caused a slight increase, of questionable significance, in the long term mortality.

22. Katz, L. N.: Electrocardiography Including an Atlas of Electrocardiograms, ed. 2, Philadelphia, Lea & Febiger, 1946.

The presence of known angina pectoris at the time of admission and up to one month preceding admission had no deleterious effect on the immediate mortality in the first two months, but the average duration of life of those who died after two months was somewhat shortened.

The presence of heart failure on admission sharply increased the immediate and over-all mortality rate and noticeably shortened the duration of life of those who died after two months. It is obvious that heart failure affects unfavorably the immediate and long term prognosis of recent myocardial infarction.

The presence of diabetes mellitus increased the mortality rate in the first two months, as well as the over-all mortality rate. However, the long term mortality rate was not greatly altered. The presence of diabetes, while not increasing the mortality rate after two months, led to an earlier death among those who died. Diabetes also reduced the duration of life of those known to have died even more strikingly in the whole group, suggesting that in the group who died within two months the ill effects occurred sooner than in the whole group. Therefore we conclude that the ill effects of diabetes manifest themselves earlier in the period after infarction and that the later prognosis is no worse than that for the entire group.

When low voltage, sinus tachycardia, heart block or ectopic rhythm was present in the electrocardiogram on admission, the mortality rate in the first two months was definitely increased, but the mortality after the first two months was not significantly altered in this group. Thus, patients in this group who survived the first two months had as good a prognosis as the entire group. The absence of low voltage, heart block, ectopic rhythms and sinus tachycardia led to a much better immediate prognosis, but the long term prognosis was no better than that for the whole group.

Patients who were symptom free on admission had an immediate mortality rate little different from that for the entire group, but the long term mortality rate was obviously better. Thus, the over-all mortality rate was less than that for the whole group. The average duration of life of those who died was considerably prolonged. Therefore we conclude that those who are asymptomatic on admission have a definitely more favorable outlook after the first two months.

The mortality rate for the first two months, after the first two months and for the entire period increased with each succeeding decade. Older patients were more adversely affected by myocardial infarction than the younger ones.

The immediate mortality rate was greater in women than in men, but after the first two months the mortality rate was less for women

than for men. However, the over-all mortality rate was higher for women than men.

Although the mortality rate in the first two months was little affected by the location of the infarct, the mortality rate after the first two months was definitely less for infarcts on the lateral wall than for those on the anterior or the posterior wall. Little difference was found in the mortality rate after two months between infarcts on the anterior and those on the posterior wall. The mortality rate was greater for the whole group when the electrocardiogram was classified as an atypical coronary pattern.

Members of the Michael Reese Hospital Staff cooperated in this study and Dr. R. Langendorf gave helpful suggestions.

Twenty-Ninth Street and Ellis Avenue (16).

Progress in Internal Medicine

GASTROENTEROLOGY

A Review of the Literature from July 1947 to July 1948

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CHICAGO

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VAGOTOMY

The tremendous interest in vagotomy is reflected in the more than seventy papers included in the present review.

From the Frank Billings Medical Clinic, Department of Medicine, University of Chicago, The School of Medicine.

Historical Aspects.—Small [501] DeCourcy [502] and Alvarez [503] present highly informative summaries of the historical aspects of this operation. Interest in the procedure apparently dates back many years, although the completeness of the vagotomy performed has been questioned by various observers.

Anatomic Relations.—Chamberlin and Winship,[504] in a necropsy study of the vagus nerves, found that in 60 per cent of bodies they fell into a simple pattern, a single trunk representing the right or posterior nerve; in 16 per cent they formed a pattern in which single trunks were formed, but two or more secondary trunks were present above the esophageal hiatus; in 12 per cent they were of a complex pattern, with more than one primary trunk.

Walters and his associates [505] and Bradley,[506] on the basis of a similar investigation, conclude that in 92 per cent of cadavers distinct right and left gastric nerves were identified at the esophageal hiatus; in 8 per cent, the arrangement of one or both gastric nerves was abnormal and irregular; identification of such nerves in gastric vagotomy would necessitate the thoracic approach. Dragstedt and his associates [507] also describe the course of the vagus nerves over the lower portion of the esophagus and present in detail their technic of transabdominal vagotomy. Doubilet and others [508] conclude that vagal section can be complete either at the infra-aortic level or at the diaphragmatic hiatus. The reviewers venture to suggest that anatomic studies, valuable as they are, do not answer the question of the incidence of completeness in vagotomy, either supradiaphragmatic or infradiaphragmatic. Accurate physiologic studies are needed not only immediately after operation but years later.

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501. Small, J. T.: Symposium on Peptic Ulcer: Denervation of the Stomach, Arch. Surg. **55**:189 (Aug.) 1947.

502. DeCourcy, J. L.: A Century and a Third of Vagotomy, Cincinnati J. Med. **29**:199, 1948.

503. Alvarez, W. C.: Sixty Years of Vagotomy: A Review of Some Two Hundred Articles, Gastroenterology **10**:413, 1948.

504. Chamberlin, J. A., and Winship, T.: Anatomic Variations of the Vagus Nerves: Their Significance in Vagus Neurectomy, Surgery **22**:1, 1947.

505. Walters, W.; Neibling, H. A.; Bradley, W. F.; Small, J. T., and Wilson, J. W.: Anatomic Distribution of the Vagus Nerves at Lower End of the Esophagus: Relation to Gastric Neurectomy for Ulcer, Arch. Surg. **55**:400 (Oct.) 1947.

506. Bradley, W. F.: Gastric Neurectomy (Vagotomy) in Treatment of Duodenal Ulcer: Anatomic Considerations, Minnesota Med. **31**:256, 1948.

507. Dragstedt, L. R.; Fournier, H. J.; Woodward, E. R.; Tovee, E. B., and Harper, P. V.: Transabdominal Gastric Vagotomy, Surg., Gynec. & Obst. **85**:461, 1947.

508. Doubilet, H.; Shafiroff, B. G. P., and Mulholland, J. H.: The Anatomy of the Peri-Esophageal Vagi, Ann. Surg. **127**:128, 1948.

Physiologic and Other Effects.—Clarke, Storer and Dragstedt [509] found that the continuous nocturnal secretion of gastric juice in the empty stomach of patients with benign ulcer is, as a rule, greater in volume than that of patients without ulcer; it is greatly reduced after section of the vagus nerves. The secretory response to insulin hypoglycemia and to a meal is abolished by the section. The pronounced decrease in gastric motility observed in the two weeks after operation disappears within one to three months.

Dragstedt and others [510] state that complete division of the vagus nerves in cases of ulcer produces complete and permanent relief of the distress. The relief is not due to anesthesia of the stomach, for the introduction of a solution of hydrochloric acid into the stomach during the first three or four days after operation reproduces the pain with its previous intensity. Trauma to the vagus nerves does not produce pain. The sensation of hunger is not abolished by complete vagotomy; inflation of a balloon in the stomach produces a feeling of distention or actual pain.

Schoen and Griswold [511] note that although basal secretion and gastric emptying were greatly decreased by vagotomy, histamine accelerated the rate of secretion and increased the concentration of pepsin and acid. The cephalic stimulus of sham feeding was noted before but not after operation, and peptic power actually decreased. Insulin-stimulated secretion was reduced. The basal secretory rate was decreased by approximately 36 per cent. Crandell and his associates [512] report a diminished response to the alcohol test meal. There was no change in the electroencephalographic pattern for patients after vagotomy, nor was there any impairment of utilization or absorption of protein.

The postoperative insulin test (ten to fourteen days after operation) yielded a negative response for acid in 22 cases, a positive response in 3 and a doubtful reaction in 1.[513] Decreased motility was observed

509. Clarke, J. S.; Storer, E. H., and Dragstedt, L. R.: The Effects of Vagotomy on the Physiology of the Stomach in Patients with Peptic Ulcer, J. Clin. Investigation **26**:784, 1947.

510. Dragstedt, L. R.; Woodward, R.; Harper, P. V., and Storer, E. H.: Mechanism of the Relief of Ulcer Distress by Gastric Vagotomy, Gastroenterology **10**:200, 1948.

511. Schoen, A. M., and Griswold, R. A.: The Effect of Vagotomy on Human Gastric Function, Ann. Surg. **126**:655, 1947.

512. Crandell, W. B.; Boehm, W. E., and Mulholland, J. H.: Effects of Supra-Diaphragmatic Section of the Vagus Nerves in Man, Arch. Surg. **55**:343 (Sept.) 1947.

513. Stein, I. F., Jr., and Meyer, K. A.: Studies on Vagotomy in the Treatment of Peptic Ulcer, Surg., Gynec. & Obst. **86**:473, 1948.

in the majority. Eight cases were restudied three to nine months after operation, with results similar to those obtained earlier, except in 1 case, in which ulcer symptoms recurred; positive secretory and motility responses to insulin were obtained.

Brody and Quigley [514] describe a method for the accurate registration of the intraluminal pressures within the upper portion of the gastrointestinal tract. An almost complete loss of so-called phasic pressure waves after vagotomy was observed in 1 case.

Monsaingeon [515] found that vagotomy did not abolish the sensation of hunger. There was no tendency toward spasm at the cardiac or pyloric orifices. Roentgenologic examination of the gallbladder, performed soon after operation in 2 cases, indicated that the gallbladder was evacuated within twenty to forty minutes; delayed evacuation of the dye was observed in 3 cases six to nine months after vagotomy.

A group of 29 patients with transthoracic section and of 4 with transabdominal resection of the vagus nerves was studied roentgenographically.[516] In the early postoperative stages there was definite gastric dilatation and atonicity in most subjects. Sluggish, ineffective and arhythmic peristalsis, or absence of peristalsis, was associated with the dilatation and atonicity. Emptying time, both initial and final, was greatly increased. The changes occurred to a lesser degree in patients with previous gastroenterostomy and in those with partial gastrectomy. There was a return toward the normal within a period of six months to a year. Complete return to normal in all respects was not observed in any case; 1 was followed for fourteen months. The ulcers, especially the stomal and jejunal ulcers, healed promptly. The postoperative size of the small bowel was not remarkable; the motility was slow, apparently because of the delay in gastric emptying. Dysphagia developed temporarily in 1 case.

Feldman and Morrison [517] suggest the possible development of a roentgenologic insulin test for the completeness of vagotomy. Mandl and Mannchen [518] describe a new test for complete vagotomy. Sym-

514. Brody, D. A., and Quigley, J. P.: Intralumen Pressures of the Stomach and Duodenum in Health and Disease, Gastroenterology **9**:570, 1947.

515. Monsaingeon, A.: Vagotomy for Ulcers, Semaine d. hôp., Paris **24**:303, 1948.

516. Ritvo, M., and Shauffer, I. A.: Roentgenographic Studies of the Gastrointestinal Tract Following Section of the Vagus Nerves for Peptic Ulcer, New England J. Med. **238**:496, 1948.

517. Feldman, M., and Morrison, S.: The Effect of Insulin on Motility of the Stomach Following Bilateral Vagotomy, Am. J. Digest. Dis. **15**:175, 1948.

518. Mandl, F., and Mannchen: Ein neuer Test für die effektiv durchgeführte Vagotomie bei Ulkuskrankheit, Wien. med. Wchnschr. **98**:97, 1948.

pathetic block on the right side at the levels of the seventh and eighth thoracic segments results in an increase in both the total acidity and the free acidity because the elimination of sympathetic stimuli results in a preponderance of vagal activity, accompanied with increased acidity and motility. The hypothesis was tested in 21 cases; the acid values increased after sympathetic block with incomplete vagotomy but remained unchanged after complete vagotomy. The procedure is therefore recommended as a test for complete vagotomy.

Transient hypertension developed after vagotomy in 2 cases.[519] Szasz [520] concludes that vagotomy provides healing of ulcer without gratification of the patient's emotional needs and that medical management should be continued for psychologic reasons, rather than for physiologic or medical reasons. The reviewers find this concept interesting but not convincing.

Clinical Results of Vagotomy.—Moses,[521] in a critical review of one hundred and forty-four papers, concludes that, although vagotomy results in "semipermanent cures," the mechanism is unknown and its permanence not yet measured. He states the belief that vagotomy should be the procedure of choice in cases of marginal ulcer and in those of duodenal ulcer penetrating into the pancreas or involving the area of the common bile duct. Ruffin and White [522] report that vagotomy affords gratifying and dramatic relief of symptoms in the majority of cases of "intractable" peptic ulcer. Recurrences have been reported in a small percentage of cases; in a few, patients have not been relieved of their symptoms. Bockus [523] adopts a conservative view. Johnson and Machella [524] and Wilbur, Cheney and Carleton [525] conclude that the operation is not indicated in gastric ulcer, that it may be indicated in duodenal ulcer, and that its principal value appears to be in ulcer recurrent after gastric resection and gastroenterostomy. Smith [526] condemns vagus section or palliative procedures for prepyloric

519. Marcussen, J. M.: Temporary Hypertension Reaction After Vagotomy, Nord. med. **38**:1222, 1948.

520. Szasz, T. S.: Psychiatric Aspects of Vagotomy: A Preliminary Report, Ann. Int. Med. **28**:279, 1948.

521. Moses, W. R.: Critique on Vagotomy, New England J. Med. **237**:603, 1947.

522. Ruffin, J. M., and White, P.: The Present Status of Vagotomy in the Treatment of Peptic Ulcer, Gastroenterology **10**:607, 1948.

523. Bockus, H. L.: Recent Advances in Treatment in Field of Gastroenterology, J. A. M. A. **136**:293 (Jan. 31) 1948.

524. Johnson, J., and Machella, T. E.: Vagotomy for the Treatment of Peptic Ulcer, Clin. North America **27**:1406, 1947.

525. Wilbur, D. L.; Cheney, G. C., and Carleton, M.: Clinical Conference of Vagotomy, M. Clin. North America **32**:301, 1948.

526. Smith, G. K.: Benign and Malignant Prepyloric Lesions of the Stomach, California Med. **68**:86, 1948.

gastric lesions, in view of the difficulty in differentiation between benign and malignant lesions. Grimson and others [527] state the conclusion that transthoracic vagotomy alone should not be used as standard treatment for duodenal or gastric ulcer, but that vagotomy may be of value when combined with gastroenterostomy or when employed for stomal ulcer.

Dragstedt [528] reports excellent results in a series of 212 cases. It is emphasized that the possibility of cancer makes the surgical problem of benign gastric ulcer different from that of duodenal or jejunal ulcer.[529] In 3 cases of coexistent gastric and duodenal ulcer and in 3 cases of ulcer high on the lesser curvature of the stomach, prompt healing was obtained after vagotomy. In the remaining 2 cases, the differential diagnosis between ulcer and cancer could not be made even at laparotomy; the ulcer failed to heal after vagotomy. The patient in 1 of these cases died of cerebral hemorrhage; there was evidence of active ulcer, but an autopsy was not obtained. The other patient, still under observation at the time of the report, had an ulcer three months later; secretory studies indicated that the vagotomy had been complete.

Moore [530] obtained satisfactory results in 90 per cent of cases. Sanders [531] confirms the conspicuous reduction in secretion, tonus, hunger contractions and relief of pain. Thorlakson [532] indicates a favorable impression with the results of 63 vagotomies. Orr and Johnson [533] describe good or excellent results in all of 34 cases of duodenal ulcer in

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527. Grimson, K. S.; Baylin, G. J.; Taylor, H. M.; Hesser, F. H., and Rundles, R. W.: Symposium on Peptic Ulcer: Clinical Evaluation of Complications Observed After Transthoracic Vagotomy, Arch. Surg. **55**:175 (Aug.) 1947.

528. Dragstedt, L. R.; Harper, P. V., Jr.; Tovee, E. B., and Woodward, E. R.: Section of the Vagus Nerves to the Stomach in the Treatment of Peptic Ulcer, Ann. Surg. **126**:687, 1947.

529. Harper, P. V., Jr., and Dragstedt, L. R.: Section of the Vagus Nerve to the Stomach in the Treatment of Benign Gastric Ulcer, Arch. Surg. **55**:141 (Aug.) 1947.

530. Moore, F. D.: Vagus Resection for Ulcer: An Interim Evaluation, Ann. Surg. **126**:664, 1947.

531. Sanders, R. L.: An Evaluation of the Methods of Surgical Treatment of Duodenal Ulcer, South. M. J. **40**:567, 1947; Bilateral Segmental Vagal Resection in the Treatment of Peptic Ulcer, ibid. **13**:493, 1947.

532. Thorlakson, P. H. T.: The Surgical Management of Chronic Duodenal Ulcer with Special Reference to the Role of Vagotomy, Canad. M. A. J. **58**:561, 1948.

533. Orr, I. M., and Johnson, H. D.: Vagal Resection in the Treatment of Duodenal Ulcer, Lancet **2**:84, 1947.

which vagotomy was regarded as complete. The outcome in 16 cases in which incomplete vagotomy was performed was recorded as fair to excellent in 12 and poor in 4. Favorable conclusions are reported by numerous authors.[534]

Vagotomy with pyloroplasty or gastroenterostomy is safer and more effective than gastric resection alone, according to Crile.[535] Gardner [536] reports good results from partial gastrectomy and vagotomy; the resection is relatively small and is performed to obviate retention after vagotomy. Franksson,[537] under the heading "Selective Abdominal Vagotomy," describes an attempt to cut branches to the upper part of the stomach, leaving the rest of the fibers intact. Postoperative insulin tests, apparently done ten days after operation, showed absence or decrease of free hydrochloric acid. The ulcer decreased in size or healed in each instance. In spite of these results, the reviewers cannot accept the rationale of the procedure because of the general observation that a single intact fiber is sufficient to activate the entire mechanism of gastric secretion. Johns and Grose [538] report an unsatisfactory outcome in 7 cases after vagotomy alone; in 3 recurrent pain occurred (in 2 the vagotomy was incomplete, as shown by insulin test), and in 3, gastric retention. Patients subjected to a combination of vagotomy and enterostomy or resection experienced uniformly good results.

534. Seabrook, D. B.: Surgical Treatment of Peptic Ulcer, Rocky Mountain M. J. **45**:26, 1948. Wulff, H. B.: Vagotomy for Peptic Ulcer: Theoretic Background and Clinical Results, Acta chir. Scandinav. **96**:265, 1947. Lowe, E. S.: Vagotomy in the Treatment of Peptic Ulcers, U. S. Nav. M. Bull. **47**:785, 1947. Cole, W. H.; Walter, L., and Reynolds, J.: Vagotomy in the Treatment of Peptic Ulcer, South. Surgeon **13**:870, 1947. Thompson, V. C., and James, A. H.: Vagotomy for Peptic Ulcer, Lancet **2**:44, 1947. Dumont, R.: Notes préliminaires sur l'opération de Dragstedt (vagotomie transthoracique), Acta gastroenterol. belg. **10**:498, 1947. Collins, E. N., and Stevenson, C. W.: Bilateral Vagotomy in the Treatment of Peptic Ulcer, Gastroenterology **10**:205, 1948. Harkins, H. N.: The Present Status of Vagotomy in Surgical Treatment of Peptic Ulcer, Northwest Med. **46**:945, 1947. Boerema, I.: Direct Results of Vagotomy in Presence of Gastric Complaints Following Operation on Account of Ulcer, Nederl. tijdschr. v. geneesk. **92**:1755, 1948.

535. Crile, G.: Transabdominal Vagotomy Versus Gastric Resection in the Treatment of Duodenal Ulcer, Cleveland Clin. Quart. **14**:264, 1947.

536. Gardner, C.: Simultaneous Vagotomy and Partial Gastrectomy for Intractable Peptic Ulcer, Canad. M. A. J. **58**:137, 1948.

537. Franksson, C.: Selective Abdominal Vagotomy, Acta chir. Scandinav. **96**:409, 1948.

538. Johns, T. N. P., and Grose, W. F.: Symposium on Vagotomy for Peptic Ulcer: II. Early Surgical Results in Forty-Three Cases, Bull. Johns Hopkins Hosp. **81**:92, 1947.

Paulson and Gladsden [539] noted no significant gastroscopic change after vagotomy except a decrease in peristaltic activity and a more patulous-appearing antrum. In those cases in which subtotal gastric resection had also been performed, the edema, nodule-like hypertrophy and friability were similar to those observed in the cases without vagotomy. Attempts to determine the influence of vagotomy on pancreatic activity by means of serum amylase levels showed no conclusive change. Important questions are raised concerning the validity and importance of the insulin test, including the difficulty of interpretation after gastroenterostomy, the problem of whether all vagal fibers can be interrupted anatomically and the possibility that all fibers need not be cut to produce satisfactory clinical results. It is concluded that relief of symptoms, decreased volume of gastric secretion, alterations in gastric tone and motility and results of the test for gastric acidity cannot be utilized as criteria for the completeness of vagotomy. Moore [540] reports that 87 per cent of 74 patients were satisfied with the results of vagotomy two to thirty months after operation. Five patients had recurrent ulcer; the side effects experienced by 5 others were of sufficient magnitude to detract from the value of the operation.

Thorek [541] performed vagotomy in 25 cases; deaths occurred in 3, none being attributable to the operation. One patient died of a perforated jejunal ulcer seven weeks after subtotal gastric resection and vagotomy. Cameron [542] reports a case in which a gastric ulcer developed, with perforation and death, sixteen days after vagotomy for chronic duodenal ulcer. In 15 cases described by Warren,[543] mild symptoms of retention were noted in 2; a recurrent duodenal ulcer with two additional gastric ulcers necessitating gastric resection developed in 1 case. Four failures were encountered by Harkins and Hooker [544] in 36 cases in which vagotomy was performed.

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539. Paulson, M., and Gladsden, E. S.: Medical Aspects of Vagotomy for Peptic Ulcer Including Observation on the Clinical Value of the Insulin Test and on Postoperative Criteria for the Completeness of Bilateral Gastric Vagus Section, Bull. Johns Hopkins Hosp. **81**:107, 1947.

540. Moore, F. D.: Resection of the Vagus Nerves for Ulcer: An Interim Evaluation, Arch. Surg. **55**:164 (Aug.) 1947.

541. Thorek, P.: Vagus Nerve Section (Vagotomy) in the Treatment of Peptic Ulcers: Review of Literature and Report of Personal Cases, J. A. M. A. **135**:1141 (Dec. 27) 1947.

542. Cameron, D. A.: Vagotomy for Peptic Ulcer, Am. J. M. Sc. **214**:202, 1947.

543. Warren, R.: Experience with Vagotomy for Peptic Ulcer, Surgery **22**:246, 1947.

544. Harkins, H. N., and Hooker, D. H.: Vagotomy for Peptic Ulcer, Surgery **22**:239, 1947.

Meyer and his associates [545] noted immediate relief from pain due to ulcer after vagotomy in 35 cases in which there had been no previous response to medical or surgical treatment. Thirty-one patients were leading an unrestricted life and were well satisfied with the results at the time of the report. One patient died of uremia and nephrosis after a blood transfusion. Recurrent symptoms with roentgenologic evidence of active ulcer developed in 4 cases, and symptoms of cardiospasm, subsiding spontaneously, were noted in 3.

Hansen [546] performed vagotomy alone or with gastroenterostomy, gastric resection or miscellaneous procedures in 52 cases. Pleural effusion occurred in all of 10 cases in which treatment was by transthoracic vagotomy. One patient died of a perforated esophagus with generalized peritonitis, aspiration pneumonia and mediastinitis on the fifth postoperative day. Abdominal distention developed in 12 cases and diarrhea, in 9. The volume of the nocturnal gastric secretion among male patients decreased from 568 to 325 cc. and among female patients from 446 to 240 cc. Postoperative roentgenologic studies indicated a persistent ulcer in 6 cases. Derom [547] noted gastric atony and dilatation in 3 of 6 cases. In 1, a gastric ulcer recurred temporarily ten months after the operation. Hallenbeck and Priestley [549] describe 2 unsatisfactory cases; pain and hemorrhage continued in 1, and gastric retention necessitated gastroenterostomy in the second. Other authors [550] express varied opinions.

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545. Meyer, K. A.: Rosi, P. A., and Stein, I. F., Jr.: Studies on Vagotomy in Treatment of Peptic Ulcer: II. Clinical Evaluation, Surg., Gynec. & Obst. **86**:524, 1948.

546. Hansen, A. M.: Vagotomy, Ann. West. Med. & Surg. **2**:249, 1948.

547. Footnote deleted on proof.

548. Derom, E.: L'atonie et la dilatation gastriques après vaguectomie de Dragstedt dans l'ulcus gastro-duodenal, Acta gastroenterol. belg. **11**:58, 1948.

549. Hallenbeck, D. A., and Priestley, J. T.: Transthoracic Vagotomy: Notes on Unsatisfactory Results in Two Cases, Proc. Staff Meet., Mayo Clin. **22**:332, 1947.

550. Illingworth, C. F. W., and Kay, A. W.: Vagotomy in the Treatment of Peptic Ulcer, Edinburgh M. J. **54**:540, 1947. Woodruff, R., and Hunter, R. T.: Indications for Vagus Nerve Resection in the Treatment of Peptic Ulcer, Rocky Mountain M. J. **44**:523, 1947. Castleton, K. B.: Vagotomy in the Treatment of Peptic Ulcer, ibid. **44**:698, 1947. Fox, S. F.: Resection of Vagus Nerves in Treatment of Peptic Ulcer, J. Maine M. A. **39**:149, 1948. Plaschkes, S. J.: Vagusresektion als Ulcusoperation, Gastroenterologia **73**:240, 1948. Orban, F., and Dalem, J.: Le place actuelle de la vagotomie dans le traitement de l'ulcère gastro-duodénale, Rev. méd. Liège **3**:129, 1948. Blackford, S. D., and McCourland, A.: Results of Vagotomy, Virginia M. Monthly **75**:265, 1948.

Walters and his associates [551] describe their experience in a series of articles, stating the conclusion that the greatest value of vagotomy is in the treatment of recurrent ulcer after partial gastrectomy. The operation is considered to have no place in the management of gastric ulcer.[551a] The relief of pain after vagotomy is attributed to the subsidence of "gastrospasm" and to the reduction of gastric acidity. The reviewers insist that "gastrospasm" is not a proved factor in pain due to ulcer, whereas the role of acidity is proved. In another article,[551d] 3 cases of ulcer symptoms are reported in which results of the insulin test were negative after vagotomy; in 2 of these, an ulcer was demonstrated roentgenologically. In another case in which the results of the insulin test were negative, an unhealed jejunal ulcer was found at operation several months after vagotomy. The authors state [551f] that they consider the results of vagotomy to be inconstant and unpredictable; they regard the procedure as in the experimental stage. Among 80 patients so treated there were 5 deaths, 4 of which were attributed to the operation. Seven patients were troubled by the persistence or recurrence of peptic ulcer or by gastric atony with pronounced retention. In a later report,[551g] the same authors review their results up to May 1, 1947, in 118 cases. Vagotomy alone was performed in 48, gastrojejunostomy having been performed previously in 14; ulcer pain persisted in 2. Vagotomy and an additional gastric operation (partial resection, pyloroplasty, gastroenterostomy or excision of gastric ulcer) were carried out in 70 patients; ulcer distress continued in 5. There were 6 deaths, 2 of which were not assigned to the operation. Recurrence of the ulcer or failure of the lesion to heal within three weeks was reported in 13 cases of the entire group. In 15 per cent of the series, symptoms of disturbed motility were noted nine months or more after vagotomy.

Comment.—Clearly, there is no unanimity of opinion concerning the present status of vagotomy. Many investigators report excellent results and advocate the procedure for treatment of all types of benign peptic

551. (*a*) Walters, W.; Neibling, H. A.; Bradley, W. F.; Small, J. T., and Wilson, J. W.: Favorable and Unfavorable Results of Gastric Neurectomy (Vagotomy) for Peptic Ulcer: An Anatomic, Physiologic and Clinical Study, S. Clin. North America **27**:885, 1947. (*b*) Walters, W.: Vagotomy for Peptic Ulcer, Proc. Staff Meet., Mayo Clin. **22**:281, 1947. (*c*) Walters, W.; Neibling, H. A.; Bradley, W. F., and Small, J. T.: A Study of the Results Both Favorable and Unfavorable of Section of the Vagus Nerves in the Treatment of Peptic Ulcer, Ann. Surg. **126**:679, 1947. (*d*) Walters, W.; Neibling, H. A.; Bradley, W. F.; Small, J. T., and Wilson, J. W.: Vagotomy in Peptic Ulcer, Minnesota Med. **30**:965, 1947; (*e*) Gastric Neurectomy for Gastric and Duodenal Ulceration, Ann. Surg. **126**:1, 1947; (*f*) Gastric Neurectomy: Anatomic and Physiologic Studies with Favorable and Unfavorable Results in Treatment of Peptic Ulcer, Arch. Surg. **55**:151 (Aug.) 1947; (*g*) Results of Vagus Nerve Resections in Treatment of Peptic Ulcer, J. A. M. A. **136**:742 (March 13) 1948.

ulcer. Others, while recording good or satisfactory results in the majority of cases, direct attention to the untoward physiologic effects encountered in occasional cases. Data on persistence and recurrence of symptoms at variable intervals after vagotomy now are being recorded; accurate correlation of these results with the completeness or incompleteness of the operation is not possible, although the impression is gained that in the majority of instances, at least, the vagus section has been incomplete. There is almost unanimous agreement in favor of vagotomy for treatment of ulcer recurrent after gastric resection or gastroenterostomy. A majority of writers seem to recommend combining the operation with gastroenterostomy for duodenal ulcer with cicatricial stenosis, although the possibility of recurrent ulcer is not excluded. Others advocate vagotomy for duodenal ulcer not responding to medical management or manifesting "vagal hyperactivity." A majority of clinicians are opposed to its use in gastric ulcer, chiefly because of the difficulties in differentiation of benign and malignant ulcer. It may also be noted, in this connection, that the principal benefit of vagotomy apparently lies in the elimination of the cephalic phase of hypersecretion; the output of acid in patients with gastric ulcer is not excessive and, indeed, is quite similar to that observed in normal persons. Vagotomy, in the opinion of the reviewers, is not a substitute for careful medical management; it should not be employed indiscriminately. Experience to date suggests, however, that vagotomy and gastroenterostomy are preferable to gastric resection in cases of chronic recurrent duodenal ulcer and high grade cicatricial stenosis. All observers agree as to the necessity of a more prolonged period of observation before the ultimate value of the operation can be assessed accurately; it is highly important, therefore, to study carefully each patient, diagnostically, clinically and physiologically.

Sympathectomy and Splanchnicectomy. — Torre and Villareal [552] describe a case of essential hypertension, in which treatment by a Smithwick sympathectomy was followed with an urge to defecate. The symptom was attributed to increased vagal effect, resulting from the section of the sympathetic nerves. Roentgenologic examination disclosed increased gastric peristalsis; six hours later the large bowel was filled with barium sulfate. Splanchnicectomy for hypertension was performed in the case of a man who had experienced "heartburn" for fifteen years; "hypermotility and spasm" of the duodenal bulb had been diagnosed roentgenologically.[553] After the operation, the heartburn disappeared;

552. Torre, J. M., and Villareal, R.: Radiological Changes in the Gastrointestinal Tract of a Patient Following the Smithwick Operation, Gastroenterology **10**:543, 1948.

553. Siris, J. H.: Amelioration of Peptic Ulcer Symptoms Following Splanchnicectomy, New York State J. Med. **48**:640, 1948.

the hypertension returned four and one-half years later. The reviewers question the interpretation of the author, who apparently relates the disappearance of the heartburn directly to the splanchnicectomy.

DUODENUM

Motility.—Mathur and his associates [554] found that hunger contractions in the duodenum of fasting dogs are temporarily inhibited by cutaneous stimuli and by the sight and smell of food. Contractions, suggesting the occurrence of reverse peristalsis from jejunum to duodenum, were recorded immediately prior to vomiting. Borisov [555] reports that denervation of the renal pedicle in dogs is followed by atony of the stomach and duodenum.

Congenital Defects.—Nelson [556] describes a congenital diaphragm of the duodenum, treated by resection.

Forshall [557] reports the cases of 4 newborn infants with duodenal obstruction, located above the ampulla of Vater in 2 and below the ampulla in 1; in the fourth case, there were a cyst of the jejunum and nonrotation and volvulus of the entire small bowel. Two of the 4 patients were operated on successfully. Stewart [558] states the belief that early vomiting of bile-stained material without abdominal distention is the essential diagnostic point. Benson and Penberthy [559] treated 2 patients satisfactorily by means of posterior gastroenterostomy and duodenojejunostomy, respectively. Patton [560] successfully treated, by longitudinal myotomy, 2 patients with congenital hypertrophic stenosis of the first portion of the duodenum. Congenital and so-called secondary and functional enlargements of the duodenum are discussed by Hillemand and Dugue.[561]

554. Mathur, P. D.; Grindlay, J. H., and Mann, F. C.: Observations on Duodenal Motility in Dogs with Special Reference to Activity During Vomiting, Gastroenterology **10**:866, 1948.

555. Borisov, M. V.: Influence of Denervation of the Renal Pedicle on the Motor Functions of the Duodenum, Khirurgiya, 1947, no. 1, p. 22.

556. Nelson, W. I.: Congenital Diaphragm of Duodenum: Case Report with Preoperative X-Ray Studies, Minnesota Med. **30**:245, 1947.

557. Forshall, I.: Duodenal Obstruction in the Newborn, Brit. J. Surg. **35**:58, 1947.

558. Stewart, J. S.: Congenital Extrinsic Duodenal Obstruction in the Newborn, South. Surgeon **14**:15, 1948

559. Benson, C. D., and Penberthy, G. C.: Congenital Duodenal Obstruction, Arch. Surg. **56**:58 (Jan.) 1948.

560. Patton, E. F.: Congenital Hypertrophic Stenosis of the Duodenum, J. Pediat. **32**:301, 1948.

561. Hillemand, P., and Dugue, M.: A propos du mégaduodénum, Arch. d. mal. de l'app. digestif. **36**:129, 1947.

Diverticula.—The various aspects of diverticula of the duodenum and jejunum are reviewed in detail.[562] Slater and Parsons[563] and Whitmore[564] conclude that diverticula of the duodenum seldom give rise to symptoms.

Cysts.—Three cases of enterogenous cyst of the duodenum are described.[565]

Arteriomesenteric Occlusion.—Metz[566] and Graver[567] both discuss the syndrome of arteriomesenteric occlusion of the duodenum with duodenal regurgitation into the stomach, characterized by recurring attacks of nausea and vomiting, with loss of weight. The positive diagnosis is based on observation of the dilated duodenum to the right of the spine, with delay of barium sulfate passing over the spine and with hyperperistalsis and regurgitation of the barium into the stomach. The reviewers continue to be highly skeptical. The syndrome, if it exists, must be extremely rare.

Duodenitis.—Diaz[568] gives a bizarre picture of duodenitis.

Removal of Foreign Bodies.—Equen and others[569] illustrate the removal of metallic foreign bodies from the duodenum by means of a magnet of aluminum, nickel, cobalt and iron, introduced under fluoroscopic guidance. Mackby[570] reports surgical removal of such a body.

Miscellaneous Disorders.—Two interesting cases are reported, 1 of perforation of the gallbladder into the duodenum, with duodenal obstruction by a gallstone, and 1 of probable congenital megaduodenum.[571] Subcutaneous retroperitoneal rupture of the duodenum after

562. Mahorner, H., and Kisner, W.: Diverticula of the Duodenum and Jejunum, Surg., Gynec. & Obst. **85**:607, 1947. D'Alotto, V.: Duodenal Diverticula, Prensa méd. argent. **34**:1696, 1947.

563. Slater, F. M., and Parsons, W. H.: The Surgical Aspects of Diverticula of the Duodenum, South. Surgeon **14**:240, 1948.

564. Whitmore, W. H.: Duodenal Diverticula with Ulceration, Am. J. Roentgenol. **59**:343, 1948.

565. Lorber, S. H., and Machella, T. E.: Enteric Cyst of the Duodenum, Gastroenterology **10**:892, 1948. Peple, W. L.: Enterogenous Cysts of the Duodenum, Ann. Surg. **127**:912, 1948.

566. Metz, A. R.: Duodenal Regurgitation, Arch. Surg. **55**:239 (Sept.) 1947.

567. Graver, F. W.: Duodenal Ileus (Wilkie's Syndrome): Arterio-Mesenteric Ileus, Bull. Vancouver M. A. **24**:116, 1948.

568. Diaz, M. J.: Observations on Duodenitis, Gac. méd. españ. **21**:233, 1947.

569. Equen, M.; Gilliam, R., and Lineback, M.: Nail in Duodenum Removed by Magnet, J. A. M. A. **135**:432 (Oct. 18) 1947. Equen, M.: Foreign Bodies in the Duodenum, South. M. J. **41**:187, 1948.

570. Mackby, M. J.: Foreign Body in Second Portion of Duodenum Perforating Pelvis of Right Kidney, J. Mt. Sinai Hosp. **14**:929, 1948.

571. Hertz, J.: Obstruction of the Duodenum with Special Reference to Gallstone Perforations, Acta chir. Scandinav. **96**:233, 1947.

trauma is reported.[572] "Pure" duodenal secretion of swine is reported to contain a factor with anti-pernicious-anemia properties.[573]

Benign and Malignant Tumors.—An adenoma of the first portion of the duodenum apparently produced the clinical features of a duodenal ulcer.[574] Fibroadenomatous benign polyps, arising in Brunner's glands, are described by Wilensky[575] and by Tedesco and others.[576] Coppla and Chimanto[577] report a polyp; Allison and Babcock,[578] a lipoma, the patient having had a history of intermittent tarry stools for two years.

The roentgenologic features of neoplasms of the duodenal and paraduodenal region are described by Kline and Culver.[579] Emphasis is placed on the presence of a small filling defect and on destruction or distortion of the mucosal pattern. Carcinoma of the duodenum is discussed by Jessen,[580] Lapeyre and others,[581] and Mendl and Tanner.[582] Poer[583] reports a lymphosarcoma of the duodenum, simulating perforated ulcer.

SMALL INTESTINE

Motility.—Helm and his associates[584] noted a definite decrease in intestinal motility after the spontaneous onset of sleep, although the degree and character of the change was not constant. Cycloheptenyl-

572. Lauritzen, G. K.: Subcutaneous Retroperitoneal Duodenal Rupture, Acta chir. Scandinav. **96**:97, 1947.

573. Landboe-Christensen, E., and Bohn, C. L. S.: On the Curative Effect of Pure Duodenal Secretion from Swine in Cases of Pernicious Anemia, Acta med. Scandinav. (supp. 205) **130**:311, 1948.

574. Swynghedauw and Salembier: Tumeur bénigne du duodénum, Presse méd. **56**:61, 1948.

575. Wilensky, A. O.: Tumors Arising in Brunner's Glands, Am. J. Digest. Dis. **15**:206, 1948.

576. Tedesco, B.; Leibovici, R., and Dausse, C.: Tumeur bénigne du bulbe duodénal, Arch. d. mal. de l'app. digestif. **37**:337, 1948.

577. Coppola, J. A., and Chimanto, A.: Polipo del duodeno, Arch. argent. de enferm. d. ap. digest. y de la nutrición **22**:256, 1947.

578. Allison, T. D., and Babcock, J. R.: Lipoma of the Duodenum Causing Melena, Ann. Surg. **127**:754, 1948.

579. Kline, J. R., and Culver, G. J.: Roentgen Findings in Primary Duodenal and Paraduodenal Malignant Lesions, Am. J. Roentgenol. **58**:425, 1947.

580. Jessen, K. E.: Duodenal Cancer, Nord. med. **35**:1651, 1947.

581. Lapeyre, N. G.; Ginestie; Groos, and Camp: Cancer of the First Portion of the Duodenum, Montpellier méd. **31-32**:5, 1947.

582. Mendl, K., and Tanner, C. H.: Carcinoma of Duodenum, Brit. J. Radiol. **21**:309, 1948.

583. Poer, D. H.: Lymphosarcoma of the Gastrointestinal Tract, Surgery **23**:354, 1948.

584. Helm, J. D.; Kramer, P.; McDonald, R. M., and Ingelfinger, F. J.: Changes in Motility of the Human Small Intestine During Sleep, Gastroenterology **10**:135, 1948.

ethyl barbituric acid (medomin®) produced relaxation of excised segments of intestine and uterus of cats and dogs; the intact intestine responded with a decrease in tonus and a lessening of rhythmic contractions.[585]

Hypermotility of the small intestine was noted in approximately 90 per cent of anesthetized dogs after rapid intravenous injections of acid and enzymatic hydrolysates, and of monosodium glutamate.[586] Solutions of amino acids with added glycine, essential for growth in rats, produced hypermotility in fewer instances (58 per cent) than did either acid and enzymatic hydrolysates or monosodium glutamate. Normal, trained dogs did not vomit after the rapid injection of growth-essential amino acids plus glycine, but emesis was common after the administration of acid hydrolysates, enzymatic hydrolysates and monosodium glutamate. The hyperglycemia which was present after rapid intravenous injections of hydrolysates or of solutions of growth-essential amino acids plus glycine largely disappeared after circulatory exclusion of the liver or after hepatectomy.

Administration of tetraethylammonium produced no change in 4 patients with cardiospasm, or in persons with a normal esophagus.[587] Intravenous injection of the drug resulted in a prompt diminution of gastric muscular tone and in generalized dilatation of the stomach, similar to that observed after vagotomy. Intravenous or intramuscular injections of the drug caused profound inhibition of the propulsive movements of the small bowel. The mucosal markings appeared to be fixed in one position over a period of minutes or hours, depending on the size of the dose. The drug produced no appreciable change in the haustral pattern of the large bowel, though it did allow the colon to become greatly distended without producing a desire to defecate. Parenterally administered, the drug appeared to block the transmission of impulses through the autonomic ganglions, both sympathetic and parasympathetic. Tetraethylammonium caused an immediate cessation, or a considerable decrease, in motility of the upper small bowel.[588] The

585. Halbeisen, W. A.; Gruber, C. M., Jr., and Gruber, C. M.: Effect of Cycloheptenylethyl Barbituric Acid, "Medomin," on Intestinal and Uterine Smooth Muscle, Proc. Soc. Exper. Biol. & Med. **68**:343, 1948.

586. Sokalchuk, A.; Ellis, D.; Wester, M. R.; Weston, K.; Greisheimer, E. M., and Oppenheimer, M. J.: Comparative Effects of Protein Hydrolysates and Amino Acid Mixtures on Intestinal Motility and Blood Sugar Levels After Rapid Intravenous Injection, Gastroenterology **10**:831, 1948.

587. Holt, J. F.; Lyons, R. H.; Neligh, R. B.; Moe, G. K., and Hodges, F. J.: X-Ray Signs of Altered Alimentary Function Following Autonomic Blockade with Tetraethylammonium, Radiology **49**:603, 1947.

588. Chapman, W. P.; Stanbury, J. B., and Jones, C. M.: The Effect of Tetraethylammonium on the Small Bowel of Man, J. Clin. Investigation **27**:34, 1948.

effect was apparently identical to that of atropine given under the same control conditions. Thresholds for intestinal pain, elicited by balloon distention, were unchanged after administration of tetraethylammonium. The value of the drug as a relaxing agent is limited by its brief duration of action.

Five antihistaminic compounds were effective, in nontoxic doses, in preventing histamine-induced spasm of the ileum in dogs.[589] The exposure, in vitro, of strips of feline small intestine to soft roentgen radiation, varying in quantity from 1,000 to 10,000 r, apparently did not influence significantly their kymographically recorded motility.[590]

Gas.—Morris, Ivy and Maddock [591] noted comparatively large intragastric and intraesophageal negative pressures during inspiration. By voluntarily relaxing the superior esophageal sphincter, air could be aspirated. It is apparent that under certain conditions, considerable amounts of air may enter the upper portion of the gastrointestinal tract without the act of swallowing.

The incidence of abdominal pain due to the expansion of intestinal gas at high altitude was studied in healthy young subjects making simulated flights to 38,000 feet (11,400 meters) in a low pressure chamber.[592] Discomfort was noted in 28.2 per cent of attempts, but distress was serious in only 5.5 per cent. Large volumes of gas were sometimes tolerated without pain. The ingestion of melons and carbonated drinks immediately before flight was consistently associated with the occurrence of pain. Diets high in carbohydrate increased the incidence and severity of pain, whereas high protein diets decreased the incidence and severity of pain. These effects were not due to an alteration in the volume of intestinal gas. In further experiments, it was found that gas immediately above or below the ileocecal valve was most likely to produce pain.

The formation of gas in the closed intestines of cats was measured after the introduction of chemotherapeutic and antibiotic agents.[593] The smallest amounts were found after the administration of penicillin and, to a lesser extent, of sulfonamide drugs; the effect of streptomyin was variable.

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589. Craver, B. N.; Cameron, A., and Yonkman, F. F.: Comparative Effectiveness of Five Antihistaminics Versus Histamine Induced Spasm in Canine Thiry-Vella Loops, J. Pharmacol. & Exper. Therap. **93**:168, 1948.

590. Craver, B. N.: The Effect of Roentgen Rays on the in Vitro Motility of Feline Intestine, Am. J. Roentgenol. **58**:357, 1947.

591. Morris, C. R.; Ivy, A. C., and Maddock, W. G.: Mechanism of Acute Abdominal Distention, Arch. Surg. **55**:101 (Aug.) 1947.

592. Blair, H. A.; Dern, R. J., and Smith, V. G.: Intestinal Gas in Simulated Flight to High Altitude, J. Aviation Med. **18**:352, 1947.

593. Schweinburg, F.; Frank, E.; Segal, A., and Fine, J.: Gaseous Distention in the Obstructed Small Intestine of Cats, Proc. Soc. Exper. Biol. & Med. **67**:45, 1947

Roentgenologic Examination.—Hodges and his associates [594a] advise against the overemphasis of the significance of minor alterations in the small bowel. In only a small percentage of cases of disorders of the small bowel can positive roentgenologic signs be found. Disease of the autonomic nerves, occurring as an isolated disorder or as one aspect of a more extensive neuropathy, may produce grave disturbances.[594b]

Diverticula, Including Meckel's Diverticulum.—In a discussion of diverticulosis of the gastrointestinal tract, Nash and Palmer [595] point out that diverticula of the first portion of the duodenum are rare, whereas pseudodiverticula secondary to ulcer spasm and scarring are common. Diverticula of the second and third portions of the duodenum are common, usually asymptomatic and rarely subject to complications but must be differentiated from neoplastic ulceration. Jejunal diverticula are rare, and usually asymptomatic. The incidence of Meckel's diverticulum is 1.5 to 3 per cent in the total population; it is twice as frequent in male as in female patients. Symptoms, when present, are usually those of obstruction or inflammation. In children, peptic ulceration with intestinal hemorrhage is the most frequent complication.

Maguire [596] reaffirms the importance of considering the presence of Meckel's diverticulum in the cases of extremely young or old patients, in which there are obscure abdominal disorders and atypical findings; the complications of acute inflammation, hemorrhage, intussusception and obstruction are discussed. Instructive reviews and case reports are presented by other writers.[597] Multiple jejunal diverticula and their complications are discussed.[598]

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594. (*a*) Hodges, F. J.; Rundles, R. W., and Havelin, J.: Roentgenologic Study of the Small Intestine: I. Neoplastic and Inflammatory Diseases, Radiology **49**:587, 1947; (*b*) II. Dysfunction Associated with Neurologic Disease, ibid. **49**:659, 1947.

595. Nash, E. C., and Palmer, W. L.: The Clinical Significance of Diverticulosis, Including Diverticulitis, of the Gastrointestinal Tract, Ann. Int. Med. **27**:41, 1947.

596. Maguire, C. H.: Meckel's Diverticulum as an Acute Surgical Emergency, Arch. Surg. **56**:65 (Jan.) 1948.

597. Messenger, H. M., and Collins, E. N.: Peptic Ulcer in Meckel's Diverticulum, Cleveland Clin. Quart. **14**:139, 1947. Murray, A. G.: A Case of Massive Hemorrhage from Peptic Ulceration in a Meckel's Diverticulum, M. J. Australia **34**:145, 1947. Olaussen, T.: Lesions in the Small Intestine Causing Melena, Nord. med. **37**:161, 1948. Taylor, S.: Symptoms Due to Meckel's Diverticulum, Lancet **2**:786, 1947. Manning, V. R., Jr., and McLaughlin, E. F.: Persistent Omphalomesenteric (Vitelline) Artery Causing Intestinal Obstruction and Gangrene of Meckel's Diverticulum, Ann. Surg. **126**:358, 1947. MacFarlane, D. A.: Foreign Body Perforations in Meckel's Diverticulum, Brit. J. Surg. **35**:421, 1948. Moses, W. R.: Meckel's Diverticulum, New England J. Med. **237**:118, 1947. Wigers, F.: Meckels divertikkel, Nord. med. **36**:2394, 1947.

598. Williams, C., and Bosher, L. H. Jr.: Jejunal Diverticulosis Complicated by the Development of Jejuno-Colic and Jejuno-Jejunal Fistulas, Ann. Surg. **127**:918, 1948. Wilkerson, J. H., and Coffman, R.: Multiple Diverticula of the Jejunum, Am. J. Surg. **75**:733, 1948.

Congenital Atresia.—Brynjulfsen [599] reviews atresia of the small and large intestine and reports 2 cases, both fatal, in which the condition was localized to the duodenum. He also reports a fatal case of multiple occurrence, and an instance of atresia of the small intestine with recovery after anastomosis. Potts [600] and O'Neill and others [601] present further instructive case reports.

Enteric Cyst.—A cyst arising from the antimesenteric border of the intestine, 3 feet (91 cm.) from the ileocecal junction, is described.[602]

Hernia.—A paraduodenal hernia was diagnosed preoperatively in the case of a patient with recurrent attacks of cramping abdominal pain and vomiting.[603] On roentgenologic examination, the intestine had the appearance of being enclosed in a round, saclike structure on the right side of the abdomen. At operation, approximately two thirds of the small intestine was found to be in a retroperitoneal hernia arising at the duodenojejunal junction.

Regional Enteritis.—Warren and Sommers,[604] in a study of 120 cases, observed obstruction of lymphatics and formation of granulomas in the intestinal wall and the lymph nodes. In the advanced or chronic state, submucosal edema, irregular hemorrhages in the mucosa and submucosa and mucosal ulceration were noted. The terminal pathologic picture included fibrosis, abscesses and fistulas.

Rachet and Busson [605] are impressed with the role of "sensitivity."

Rossmiller and Messenger [606] reviewed the findings in 55 cases of regional enteritis; follow-up studies were made in 40. Cramping abdominal pain, weight loss and diarrhea were the outstanding symptoms. The most common objective findings were a palpable mass, usually located in the right lower quadrant of the abdomen, fever, a

599. Brynjulfsen, B. C.: Intestinal Atresia, Nord. med. **36**:2401, 1947.

600. Potts, W. J.: Congenital Atresia of Intestine and Colon, Surg., Gynec. & Obst. **85**:14, 1947.

601. O'Neill, J. F.; Anderson, K.; Bradshaw, H. H.; Lawson, R. B., and Hightower, F.: Congenital Atresia of the Small Intestine in the Newborn: Report of Two Cases, with Review of Successfully Treated Intrinsic Obstructions of Small Bowel, Am. J. Dis. Child. **75**:214 (Feb.) 1948.

602. Tedesco, V. E., and Connell, J. H.: Enteric Cyst, Am. J. Surg. **74**:226, 1947.

603. Reeves, R. J.; Moran, F. T., and Jones, P. A.: Right Paraduodenal Hernia with Roentgen Diagnosis and Postoperative Recovery, Am. J. Roentgenol. **59**:338, 1948.

604. Warren, S., and Sommers, S. C.: Cicatrizing Enteritis (Regional Ileitis) as a Pathologic Entity, Am. J. Path. **24**:475, 1948.

605. Rachet, J., and Busson, A.: Entérite et entérocôlite folliculaire et segmentaire, Acta gastroenterol. belg. **11**:192, 1948.

606. Rossmiller, H. R., and Messenger, H. M.: Regional Enteritis: Diagnosis and Treatment; a Study of Fifty-Five Cases Over a Nine-Year Period, M. Clin. North America **32**:419, 1948.

draining sinus of the abdominal wall and/or a fistula in ano. Short circuiting operations without transection of the bowel distal to the anastomosis and proximal to the diseased segment proved unsatisfactory; favorable results were obtained after resection. Appelmans and his associates [607] conclude, after a review of 40 cases, that the most satisfactory treatment is wide resection in a single stage procedure.

A fatal instance of enterocolitis, involving both the small and large intestine, is reported in a child of 1 month.[608] Histologic demonstration of chronic inflammation, fibrosis and hypertrophy of the bowel suggested that the process had begun in utero.

The occurrence of regional enteritis in 2 members of the same family, father and son, is described by Kirsner and others.[609] Other interesting cases are reported.[610] In the case of a patient with extensive chronic enteritis involving the jejunum, ileum and colon, miliary and submiliary tubercles with caseation were observed in the liver, spleen, lungs, adrenals and mesenteric lymph nodes at autopsy.[611] Acid-fast organisms resembling tubercle bacilli were found in some of these lesions, but a primary focus was not demonstrated. The propriety of classifying this condition as "regional enteritis" seems debatable.

Osteomalacia was present in all of 16 cases in male patients with regional enteritis [612]; the process was mild in 36 per cent, moderate in 55 per cent and pronounced in 9 per cent. A similar finding was noted in 71 per cent of 7 cases in female patients. Regional enteritis involving segments of the entire small bowel, diagnosed at laparotomy, apparently subsided under conservative management, including the administration of penicillin and streptomycin.[613] The subject is reviewed by Merke [614] and by Hillemand.[615]

607. Appelmans, R.; Van Goidsenhaven, P., and Fannes: De ileitis van Crohn, Konink. Vlaamse Acad. v. geneesk. Verhandl. **9**:425, 1947.

608. Koop, C. E.; Perlingiero, J. G., and Weiss, W.: Cicatrizing Enterocolitis in a New Born Infant, Am. J. M. Sc. **214**:27, 1947.

609. Kirsner, J. B.; Owens, F. M., and Humphreys, E. M.: Regional Enteritis in Father and Son, Gastroenterology **10**:883, 1948.

610. Forney, J. M.; Eskridge, M., and Shaver, J. S.: Regional Enteritis, South. M. J. **40**:732, 1947. Raffensperger, E. C.: Recurrence of Regional Ileitis Associated with Pregnancy, Gastroenterology **10**:1010, 1948. Janus, W. L.: Regional Jejunitis, Radiology **50**:532, 1948.

611. Gould, S. F.: A Case of Regional Enteritis, Am. J. Clin. Path. **17**:955, 1947.

612. Bonorino Udaondo, C., and Castex, M. R.: Ileítis regional y trofismo óseo, Prensa méd. argent. **34**:1523, 1947.

613. Corbett, R. A.: Regional Ileitis Treated with Streptomycin, Rocky Mountain M. J. **44**:821, 1947.

614. Merke, F.: Weitere Beobachtungen über die Ileitis terminalis, Schweiz. med. Wchnschr. **77**:751, 1947.

615. Hillemand, P.: L'iléite terminale, Presse méd. **56**:424-A (June 16, supp.) 1948.

Hirschberg [616] notes a similarity between the symptoms of chronic enteritis and those of the postgastroenterostomy syndrome.

Acute Jejunitis.—Brekke [617] describes 9 cases of phlegmonous lesions of the small intestine, including 5 involving the terminal ileum. One case, given in detail, is that of a girl of 10; at operation, involvement was observed from the ligament of Treitz to the middle of the small intestine. No resection was attempted. Biopsy of a node revealed nonspecific inflammation, and culture yielded hemolytic streptococci. The use of penicillin apparently led to recovery. In 14 cases in which the diagnosis was acute jejunitis,[618] the roentgen signs were reduced movement of one or both sides of the diaphragm, distended loops of small bowel with fluid levels, persistently irregular pattern of the jejunal mucosa and delayed emptying of the affected loops. Twenty-one cases of acute jejunitis and 16 of acute regional enteritis are described.[619] The author states the belief that acute jejunitis occurs more frequently than is recognized. Jejunitis is classified as acute phlegmonous jejunitis, with a high mortality, and as acute simple jejunitis, with a low mortality. Pyogenic bacteria are apparently of etiologic importance.

Nonspecific Ulcers.—Evert and others [620] state that nonspecific ulcers of the jejunum and ileum are characteristically solitary, although small groups are sometimes found. The etiology is unknown; there is little direct evidence to support the theories that the lesion is caused by infection, irritation from gastric secretions, trauma or vascular abnormalities. The symptoms are, for the most part, secondary to the complications of perforation, bleeding or obstruction. The mortality rate is high. The lesion has been recognized during life only after complication has led to surgical intervention. An additional case is described by Dumont.[621]

Tuberculosis.—Schaffner [622] reports a series of 109 consecutive cases of pulmonary tuberculosis in which the patients were operated on for acute or subacute abdominal conditions; 101 cases suggested the diag-

616. Hirschberg, F.: Enteritis chronica-jejunitis and ileitis, Nord. med. **36:** 2499, 1947.

617. Brekke, A.: Jejuno-ileitis phlegmonosa, Nord. med. **34:**827, 1947.

618. Husebye, O. W.: On Roentgenological Diagnosis of "Jejunitis Acuta Phlegmonosa," Acta radiol. **29:**71, 1948.

619. Brynjulfsen, B. C.: Jejunitis acuta-ileitis regionalis acuta, Acta chir. Scandinav. **96:**361, 1948.

620. Evert, J. A.; Black, B. M., and Dockerty, M. B.: Primary Nonspecific Ulcers of the Small Intestine, Surgery **23:**185, 1948.

621. Dumont, R.: Hémorrhagie massive par ulcère simple du grêle, Acta gastroenterol. belg. **10:**112, 1947.

622. Schaffner, V. D.: Intestinal Tuberculosis, Canad. M. A. J. **57:**561, 1947.

nosis of acute appendicitis and 8, that of obstructive lesions. Of the 101 patients with symptoms of appendicitis, 20 (19.8 per cent) were found to have tuberculosis of the appendix or of the ileocecal region.

The incidence of intestinal tuberculosis discovered at necropsy in cases of active pulmonary tuberculosis was 28 per cent.[623] The incidence of intestinal perforation was 10.4 per cent and of obstruction, 12.5 per cent. A case of hyperplastic tuberculosis of the colon is described in a woman of 26, with a history of pleurisy and tuberculous lymphadenitis.[624] At operation, the lesion was thought to represent cancer; histologic examination disclosed the correct diagnosis.

Sweany[625] reports subjective improvement due to streptomycin in 2 proven cases and 9 suspected cases of tuberculous enteritis. Markoff[626] presents a preliminary report of 5 cases; however, the follow-up period was only six months.

Intestinal tuberculosis is comprehensively reviewed in twenty additional articles.[627]

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623. Kornblum, S. A.; Tale, C., and Aronson, W.: Surgical Complications of Intestinal Tuberculosis as Seen at Necropsy, Am. J. Surg. **75**:498, 1948.

624. Brodin, H.: Case of Multiple Hyperplastic Tuberculosis of the Colon, Acta radiol. **28**:227, 1947.

625. Sweany, H. C.: Streptomycin in Tuberculous Enteritis, Am. Rev. Tuberc. **56**:415, 1947.

626. Markoff, N.: Die Streptomycinbehandlung der Darmtuberkulose, Schweiz. med. Wchnschr. **78**:329, 1948.

627. Brohee, G., and Everaets, P.: Radiologie et tuberculose iléo-cécale, Acta gastroenterol. belg. **10**:143, 1947. Warmoes, F., and Gyselen, A.: La tuberculose jejuno-iléo-cécale: Point de vue clinique, ibid. **10**:163, 1947. Courtois, R.: La tuberculose jejuno-iléo-cécale: Point de vue social, ibid. **10**:185, 1947. Tilmont, L.: La tuberculose jejuno-iléo-cécale: Point de vue radiologique, ibid. **10**:193, 1947. Van der Hoeden, R.: La tuberculose jejuno-iléo-cécale: Point de vue biologique, ibid. **10**:205, 1947. Firket, J., and Scaville, A.: La tuberculose jejuno-iléo-cécale: Point de vue biologique; B. Anatomo-pathologie et bacteriologie, ibid. **10**:219, 1947. Goffin, R.: La tuberculose jejuno-iléo-cécale: Thérapeutiques spéciales et chirurgie, ibid. **10**:233, 1947. Maisin, J.: La tuberculose jejuno-iléo-cécale: Thérapeutiques spéciales; B. radiothérapie, ibid.**10**:249, 1947. Michez, J.: La tuberculose jejuno-iléo-cécale: Thérapeutiques spéciales; C. physiothérapie, ibid. **10**:257, 1947. Warmoes, F.; DeWinter, L., and Gyselen, A.: La tuberculose jejuno-iléo-cécale; Conclusions générales, ibid. **10**:269, 1947. Warmoes, F.: La tuberculose jejuno-iléo-cécale: Expériences personnelles du traitement de la tuberculose intestinale sécondaire par les rayons ultra-violets, ibid. **10**:302, 1947. Wilkinson, M. C.: Intestinal tuberculosis, ibid. **10**:313, 1947. Baumel, J.: Quelques réflexions à propos de la tuberculose hypertrophique du cécum diagnostiquée et operée comme cancer cécal, ibid. **10**:315, 1947. Haak, A.: Quelques mots sur la tuberculose iléo-cécale, ibid. **10**:321, 1947. Rachet, J.; Busson, A., and Arnous, J.: Intérêt du peristaltisme provoqué dans le diagnostic radiologique de la tuberculose iléo-cécale, ibid. **10**:324, 1947. Stephani, J.: Radiologie et clinique

(Footnote continued on next page)

Steatorrhea and Sprue.—Adlersberg and Schein[628] describe 36 cases of "primary" sprue and 4 of steatorrhea secondary to other diseases. Four hundred cases of tropical sprue are reviewed by Elder.[629] The highest seasonal incidence in India, Assam and Burma is during May, June and July. Sprue may develop after only a short stay in the tropics. Fully established sprue may be present in the absence of steatorrhea. Treatment consisted in frequent small feedings of a diet low in fat, supplemented with nicotinic acid, riboflavin and liver.

Black and his associates[630] carried out fat balance studies on 28 patients with early tropical sprue, determining percentage of fat absorbed by the expression $\frac{\text{dietary fat} - \text{fecal fat}}{\text{dietary fat}} \times 100$. In untreated sprue, fat absorption ranged from 51 per cent to 85 per cent, the normal being 90 per cent. Administration of nicotinic acid and riboflavin did not bring about improvement. After treatment with liver, improvement in fat absorption was not appreciable for some weeks. When yeast extract was given by mouth in large doses, some improvement occurred within twelve days. In a study of 30 early cases in Karachi, India, Howell[631] noted a high ratio of split fat to unsplit fat in most instances. During recovery the total amount of fecal fat often returned rapidly to normal limits, but the ratio lagged behind by one or two months.

In a series of 45 cases of idiopathic steatorrhea studied by Cooke and others,[632] 33 patients had a red cell count above 2,500,000 per cubic millimeter and hemoglobin values exceeding 50 per cent. Ten had leukopenia. Of 17 sternal punctures, 4 were indistinguishable

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de la tuberculose intestinale, ibid. **10**:327, 1947. Bernard, A.: Sûr un cas de tuberculose de l'intestin grêle, ibid. **10**:330, 1947. Bernard, A.: Tuberculose annexielle et intestinale, ibid. **10**:334, 1947. Delannay, E.: Evolution et ordre d'apparition des lésions tuberculeuses iléales et iléo-cécales, ibid. **10**:339, 1947. Vaccarezza, R. F.; Goñi-Moreno, I.; Fernandez-Luna, D.; Stapler, N. B.; Capurro, F. G., and Nunez, C. G.: Etiologia, anatomia patologica, diagnostico clínico, y radiológico y tratamiento de la tuberculosis intestinal, Rev. Asoc. méd. argent. **62**:175, 1948.

628. Adlersberg, D., and Schein, J.: Clinical and Pathologic Studies in Sprue, J. A. M. A. **134**:1459 (Aug. 23) 1947.

629. Elder, H. H. A.: Clinical Features, Diagnosis, and Treatment of Sprue, J. Trop. Med. **50**:212, 1947.

630. Black, D. A. K.; Bound, J. P., and Fourman, L. P. R.: Fat Absorption in Tropical Sprue, Quart. J. Med. **16**:99, 1947.

631. Howell, C. A. H.: An Early Sign in Sprue, Lancet **2**:55, 1947.

632. Cooke, W. T.; Frazer, A. C.; Peeney, A. L. P.; Sammons, H. G., and Thompson, M. D.: Anomalies of Intestinal Absorption of Fat: II. The Hematology of Idiopathic Steatorrhea, Quart. J. Med. **17**:9, 1948.

from those in pernicious anemia. Slight bilirubinemia was present in 8 patients. Free hydrochloric acid was present in the gastric content of 31 of 42 patients. Response to treatment with liver varied. The authors conclude that the macrocytic anemia of steatorrhea cannot be explained by the unitarian theory generally accepted in macrocytic anemias. In a study by Innes[633] of the peripheral blood of 63 patients with the sprue syndrome, the characteristic picture in the adult was macrocytosis, with or without anemia. Macrocytosis tended to persist in spite of liver therapy. Hypochromic microcytic anemia was noted in celiac disease. In 9 of 18 cases in adults, the bone marrow was megaloblastic; the marrow was normoblastic in the 2 cases of celiac disease reported.

Observations on 6 patients with sprue during seven remissions following therapy with pteroylglutamic acid are summarized.[634] Each was characterized by relief of glossitis, with regeneration of lingual papillae, cessation of diarrhea, gain in weight and hematologic improvement. In 5 instances, a return toward a normal glucose tolerance was demonstrated. Improved absorption of vitamins and increased prothrombin concentration were noted. Two patients relapsed when administration of pteroylglutamic acid was withdrawn. Five milligrams of folic acid (pteroylglutamic acid) adequately maintained a patient with sprue.[635]

Parasites were found in the feces of 56 per cent of 25 patients with tropical sprue[636]; Trichuris trichiura and Necator americanus were the most common. The patients improved after the administration of folic acid, without antiparasitic therapy.

Contrary results are reported by Weir and Comfort.[637] Administration of folic acid, usually 50 mg. daily by the intramuscular route, did not cause improvement in the sense of well-being or in gain in weight or strength in 5 cases. The frequency or severity of the exacerbations did not change; the anemia and macrocytosis persisted.

Osteomalacia secondary to steatorrhea in a woman of 61 progressed despite treatment with a low fat diet, supplemented with viosterol

633. Innes, E. M.: The Blood and Bone Marrow in the Sprue Syndrome, Edinburgh M. J. **55**:282, 1948.

634. Darby, W. J.; Jones, E.; Warden, H. F., and Kaser, M. M.: Influence of Pteroylglutamic Acid on Gastrointestinal Defects in Sprue, J. Nutrition **34**:645, 1947.

635. Vedder, E. B.: A Case of Sprue Maintained on Folic Acid, Am. J. Trop. Med. **27**:723, 1947.

636. Milanes, F.; Spies, T. D.; Hernandez Beguerie, R., and Garcia Lopez, G.: Some Observations on the Effect of Synthetic Folic Acid on the Alimentary Tract of Patients with Tropical Sprue, Rev. Gastroenterol. **15**:33, 1948.

637. Weir, J. F., and Comfort, M. W.: Folic Acid Therapy in Nontropical Sprue: Results of Treatment in Seven Cases, J. Lab. & Clin. Med. **32**:1231, 1947.

(irradiated ergosterol) and calcium.[638] The parenteral administration of viosterol resulted in greater retention of calcium and in a rise in the blood calcium level.

Glass [639] concludes that the "small intestinal deficiency pattern" may be caused by many factors other than a deficiency of vitamin B complex. Instances of prepyloric, pyloric and postpyloric lesions are described, in which disordered motor function of the small intestine was observed without specific disease of the small intestine.

Absorption of Fat.—Folic acid was shown to be of no value in improving the absorption of fat and nitrogen in dogs deprived of external pancreatic secretion.[640] Resection of the mesenteric lymph nodes in 10 dogs did not alter fecal fat and nitrogen excretion.[641] In each dog, there was rapid reestablishment of anatomic and functional continuity of the mesenteric lymphatics. Partial regeneration of the nodes occurred in 6 animals. Alimentary lipemia curves were normal six to twelve days after operation in 3 of 4 dogs examined.

Absorption and Transport of Iron.—Gillman and Ivy,[642] in studies on guinea pigs, found that ferrous iron is converted into ferric iron immediately on contact with the saliva; it is conducted through the intestinal canal and is absorbed by the epithelium in ferric form. The mononuclear phagocytic reticuloendothelial cells and the lymphatics are prominent in transporting iron from the intestine to the associated mesenteric lymph node. The histologic changes occur in at least three phases: In the first, the iron may be distinguished in the lumen of the bowel; nongranular, prussian blue–positive material can be seen clearly in the base of the epithelium. This form of iron occurs during the first one to one and a half hours after feeding iron. The second phase commences between three and six hours after feeding; there is an increase in the number of fine iron-containing granules in the luminal pole of the epithelial cells and in the amount of prussian blue–positive material immediately below the cuticular border. The third phase,

638. Fourman, L. P. R., and Spray, G. H.: Absorption of Vitamin D in Steatorrhea, Brit. M. J. **1**:142, 1948.

639. Glass, W. H.: Non-Vitaminic Factors Involved in the Production of the "Small Intestinal Deficiency Pattern," Gastroenterology **10**:660, 1948.

640. Douglas, G. F., Jr., and Pratt, T. D.: Fat and Nitrogen Absorption After Folic Acid Administration in Dogs Deprived of External Pancreatic Secretion, Proc. Soc. Exper. Biol. & Med. **68**:171, 1948.

641. Clarke, B. G.; Ivy, A. C., and Goodman, D.: Effect of Resection of Mesenteric Lymph Nodes on Intestinal Fat Absorption in the Dog, Am. J. Physiol. **153**:264, 1948.

642. Gillman, T., and Ivy, A. C.: Histological Study of the Participation of the Intestinal Epithelium, the Reticulo Endothelial System and the Lymphatics in Iron Absorption and Transport, Gastroenterology **9**:162, 1947.

initiated eight to twenty-four hours after feeding, continues for at least twenty-four to forty-eight hours. During this phase, iron cannot be detected in the cuticular border or in the lumen of the bowel. However, it can be seen in the epithelial cells, in both the granular and the nongranular (or diffuse) form, in the luminal half of the cells. Eight hours after feeding, there is an increased amount of iron in the phagocytes in the villi; these are practically confined to the tips of the villi, capping the lacteals and occasionally invading the epithelium.

Intestinal Lipodystrophy.—Three cases of presumptive intestinal lipodystrophy (Whipple's disease), in which the patients were operated on because of an indefinite abdominal mass and in which the condition was diagnosed on the basis of the appearance of the mesentery at operation, are reported.[643]

Endometriosis.—In two excellent papers, McGuff and his associates[644] review 16 cases of endometriosis causing intestinal obstruction and 48 similar cases described in the literature. The patients were largely between the ages of 30 and 50. The majority were sterile. Sigmoidoscopic examination revealed the lesion in 9 of 12 cases; roentgenograms of the colon revealed the process in 9 of 11 cases. The most important points in diagnosis are: acquired dysmenorrhea, menstrual irregularity, sterility, rectal or pelvic pain, absence of loss of weight, the presence of associated uterine fibroids or ovarian cysts and a long history of symptoms referable to the intestine and suggestive of progressive intestinal obstruction, with frequent exacerbations at menstruation. Severe constipation, pain low in the abdomen and abdominal distention are almost always present. Diarrhea is occasionally a symptom; gross blood in the feces is infrequent. The finding of a firm tumor in the rectovaginal septum or of tender palpable nodules, plus the palpation of uterine fibroids and bilateral ovarian cysts, is suggestive of endometriosis. The treatment is surgical, consisting usually of panhysterectomy, with or without temporary colostomy, as is deemed necessary. For a younger woman, with a discrete endometrioma of the ileum or of the sigmoid causing obstruction, resection of the intestine without oophorectomy is indicated. Ileal obstruction usually is due to kinking caused by the endometriosis, while the obstruction in the sigmoid and in the lower part of the intestine more often is due to an impingement of the endometrioma into the lumen of the intestine.

643. Pemberton, J. deJ.; Comfort, M. W.; Fair, E., and Zaslow, J.: Intestinal Lipodystrophy (Whipple's Disease), Surg., Gynec. & Obst. **85**:85, 1947.

644. McGuff, P.: Endometriosis as a Cause of Obstruction of the Intestine, Proc. Staff Meet., Mayo Clin. **23**:215, 1948. McGuff, P.; Dockerty, M. B.; Waugh, J. M., and Randall, L. M.: Endometriosis as a Cause of Intestinal Obstruction, Surg., Gynec. & Obst. **86**:273, 1948.

Sutler [645] reports involvement of the intestinal tract in 35 of 848 cases of endometriosis (4.13 per cent). Of these, the appendix was affected in 25, the rectosigmoid, in 9, and the ileum, in 1. Involvement of the bowel occasionally simulates malignancy. Intussusception occurred in a woman of 23 [646]; early obstruction, in a housewife of 44.[647]

Intussusception.—Among 129 cases of intestinal invagination, 28 were in children from 3 to 15.[648] Failure to recognize acute intussusception is the chief cause of death.[649] Spontaneous passage of blood was the initial manifestation in only 4 of 100 cases. Vomiting and spasmodic pain are frequent early symptoms.

Dennis [650] performed 8 successful resections in children. McLaughlin [651] concludes that recovery in children under 1 year is unusual.

Two cases are reported of spontaneous chronic intussusception of the ileum into the cecum in adults, both relieved by barium sulfate enemas.[652] The onset of symptoms was acute and was followed with chronic periodic abdominal pain and diarrhea. One patient underwent an appendectomy three months before the diagnosis of intussusception was made. In 1 case, intussusception was due to a solid tumor of aberrant pancreatic tissue, 15 cm. from the ileocecal valve [653]; multiple intussusception of traumatic origin is reported.[654]

Experimental intussusception in dogs was reduced by 3 feet (91 cm.) of saline hydrostatic pressure when the process was of less than thirty-eight hours' duration.[655]

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645. Sutler, M. R.: Endometriosis of the Intestinal Tract, Surgery **22**:801, 1947.

646. Southern, E. M.: Aberrant Endometrial Tissue and Intussusception, Brit. M. J. **1**:1178, 1948.

647. Katz, A. B.: Endometriosis of the Ileum, Am. J. Digest. Dis. **15**:162, 1948.

648. Duhamel, B.: Les aspects anatomo-cliniques des invaginations intestinales et en particulier des invaginations du côlon transverse chez les infants de plus de trois ans, Presse méd. **55**:499, 1947.

649. Morrison, B., and Court, D.: Acute Intussusception in Childhood, Brit. M. J. **1**:776, 1948.

650. Dennis, C.: Resection and Primary Anastomosis in the Treatment of Gangrenous or Non-Reducible Intussusceptions in Children, Ann. Surg. **126**:788, 1947.

651. McLaughlin, C. W., Jr.: Surgical Management of Irreducible Intussusception, Arch. Surg. **56**:48 (Jan.) 1948.

652. Hansen, P. B.: On Spontaneous Chronic Intestinal Invagination in Adults, Acta radiol. **28**:115, 1947.

653. Bosworth, B. M., and Stein, H. D.: Intussusception in Adults, Am. J. Surg. **74**:801, 1947.

654. Falor, W. H.: Multiple Intussusceptions, Direct and Retrograde, of Traumatic Origin, Ann. Surg. **127**:730, 1948.

655. Ravitch, M. M., and McCune, R. M., Jr.: Reduction of Intussusception by Hydrostatic Pressure, Bull. Johns Hopkins Hosp. **82**:550, 1948.

Intestinal Obstruction.—Case [656] advocates the use of umbrathor,® an aqueous preparation of thorium dioxide, for the roentgenologic examination of patients with acute or chronic obstruction. The potential danger from the use of barium sulfate is avoided; the material effectively aids in determining the site and extent of the lesion.

Osgood [657] presents a detailed and instructive discussion of the roentgenologic features of intestinal obstruction, with particular reference to the use of the Miller-Abbott tube. Roentgenographic findings were conclusive in 94 of 100 cases.[658] Adhesions were responsible for 78 per cent of the obstructions. The importance of a "scout film," to be followed by special views only as necessary, is stressed. Frimann-Dahl [659] discusses, in considerable detail, the roentgenologic features of mechanical and paralytic ileus. Repeated examination is advocated in cases in which the roentgenologic findings are inconclusive.

Six cases of adynamic ileus are reported by Leithauser.[660] The distention was not controlled by mechanical decompression or by the administration of neostigmine methylsulfate U. S. P. (prostigmin methylsulfate®) but seemed to respond dramatically to the administration of thiamine hydrochloride and vitamin B complex. It seems to the reviewers that more evidence is needed before the concept of nutritional ileus can be accepted.

Zuelzer and Wilson [661] describe 11 cases in which the clinical picture was that of acute, recurrent or chronic intestinal obstruction, for which no mechanical cause was demonstrable. Autopsy in 5 cases revealed an absence of the myenteric plexus in the distal portion of the intestinal tract, which correlated to a fair degree with the level of "obstruction."

Two interesting cases are reported in which torsion of the small bowel occurred through congenital mesenteric defects [662]; the patients in both cases died of shock. A total of 97 similar cases have been described in the literature; the mortality rate among 73 of the group

656. Case, J. T.: Umbrathor as a Substitute for Barium in the Roentgen Study of Acute Intestinal Obstruction, Am. J. Roentgenol. **58**:422, 1947.

657. Osgood, E. C.: The Role of the Radiologist in the Management of Patients with Intestinal Obstruction, with Special Reference to the Use of the Miller-Abbott Tube, Radiology **49**:529, 1947.

658. Spencer, J., and Thaxter, L. T.: Acute Obstruction of the Small Bowel, Radiology **49**:611, 1947.

659. Frimann-Dahl, J.: Roentgenological Examinations of Ileus, Acta radiol. **28**:331, 1947.

660. Leithauser, D. J.: Atypical Adynamic Ileus Apparently Caused by Nutritional (Thiamine Chloride) Deficiency, Surg., Gynec. & Obst. **86**:543, 1948.

661. Zuelzer, W. W., and Wilson, J. L.: Functional Intestinal Obstruction on a Congenital Neurogenic Basis in Infancy, Am. J. Dis. Child. **75**:40 (Jan.) 1948.

662. Vuori, E. E.: Two Cases of Incarceration in a Defect in the Mesentery of the Small Intestine, Acta chir. Scandinav. **95**:541, 1947.

was 33 per cent. De Nicola[663] describes obstruction produced by multiple thrombi in the small radicles of the mesenteric veins. Spackman[664] emphasizes the danger of irradiation injury to the small bowel and the sigmoid in the treatment of cancer of the uterus and cervix. Intraperitoneal adhesions, resulting from the injection treatment of an inguinal hernia, caused fatal obstruction.[665] Obstruction complicated a seven month pregnancy.[666] Ileus followed cesarean section.[667] A schizophrenic patient recovered uneventfully after the surgical removal of two teaspoons, three toothbrushes, two nails, wool fibers, a wood splinter and a piece of moleskin cloth, in addition to the appendix, from the gastrointestinal tract.[668]

Patients have survived the removal of bezoars,[669] orange pulp[670] and accumulations of ascaris.[671]

Interesting cases of gallstone ileus are described by Lace,[672] Meiselas,[673] Kapel,[674] and Minty and others.[675]

Macnab,[676] and Cole[677] review the classification, pathology, symptomatology and treatment of acute intestinal obstruction. The decreasing mortality rate is attributed to early diagnosis, intelligent use of gastrointestinal decompression, careful attention to fluid, electrolyte and protein balance and improved operative technic. The importance of

663. De Nicola, R. R.: Unusual Findings in the Ileocecal, Appendiceal Region, Northwest Med. **46**:519, 1947.

664. Spackman, J. G.: Obstructive Lesions of the Small Intestine and Sigmoid Due to Irradiation, Ann. Surg. **127**:121, 1948.

665. Lawrence, K. B.: Fatal Intestinal Obstruction Following Injection Treatment of an Inguinal Hernia, New England J. Med. **238**:397, 1948.

666. Siegel, S. A., and Pleshette, N.: Intestinal Obstruction Complicating Pregnancy, New York State J. Med. **48**:1264, 1948.

667. Neff, G.: Ileus nach Schnittentbindung, Schweiz. med. Wchnschr. **77**:755, 1947.

668. Schantz, B. A., and Kamil, R. S.: Mechanical Intestinal Obstruction, New York State J. Med. **47**:2605, 1947.

669. Watt, C. H., and Harner, J. W.: Bezoars Causing Acute Intestinal Obstruction, Ann. Surg. **126**:56, 1947.

670. Baumeister, C. F., and Darling, D. D.: Acute Intestinal Obstruction Due to Orange Pulp Bezoar, Ann. Surg. **126**:251, 1947.

671. Verhaege, E.: Acute Intestinal Obstruction Caused by Ascaris, Lille chir. **2**:112, 1947.

672. Lace, T.: Gallstone Ileus, Am. J. Surg. **74**:86, 1947.

673. Meiselas, D. A.: A Case of Gallstone Ileus, Rev. Gastroenterol. **14**:857, 1947.

674. Kapel, O.: Operative Treatment of Gallstone Ileus Without Enterostomy, Acta chir. Scandinav. **95**:54, 1947.

675. Minty, E. W.; McHaffie, O. L., and Wells, A. H.: Diagnostic Case Study, Minnesota Med. **31**:656, 1948.

676. Macnab, D. S.: Acute Intestinal Obstruction, Canad. M. A. J. **57**:371, 1947.

677. Cole, W. H.: Intestinal Obstructions, Canad. M. A. J. **58**:241, 1948.

correcting fluid and electrolyte imbalance and hypoproteinemia in acute obstruction of the small bowel is again emphasized.[678] Crile[679] also stresses the importance of intubation with the Miller-Abbott or Harris tube and the restoration of fluid and electrolyte balance. Baumgartner[680] states that delay in operation may be attributed to the "calming influence of indwelling siphonage both on the patient and on the surgeon."

Tendler and his associates[681] report an over-all mortality of 26 per cent. The elapsed time factor is apparently of prime importance, since more than 50 per cent of the patients who died had come to the hospital four days or more after the onset of symptoms, whereas of 555 patients admitted within twenty-four hours after the onset of symptoms, only 10.5 per cent died.

Skjold[682] reports a mortality rate of 27 per cent in 148 consecutive cases. Persistent postoperative paralytic ileus was relieved by cecostomy.[683]

Viability of Strangulated Bowel.—Laufman and Method[684] studied the role of vascular spasm in the recovery of strangulated bowel. Release of strangulation of the arterial type was followed by reactive hyperemia and then by a phase of vasospasm. Release of viable strangulation of the venous type was followed by a slow rise in temperature to a control level. Release of strangulation in nonviable bowel resulted in "poor" temperature response. Administration of papaverine hydrochloride, warm packs, oxygen inhalation, and mesenteric injections with procaine hydrochloride U. S. P. (novocain®) were of value in releasing residual vasospasm. Lichtenstein[685] states that he regards observation of change in the color of the bowel concomitantly with the inhalation of 100 per cent oxygen as one of the most delicate tests for viability of the bowel. The immediate transition of a dusky colored bowel to a bright pink is an indication that blood is circulating through the wall of the bowel, and viability is assured.

678. Efskind, L.: A Clinical Study of the Hematological Changes in Acute Obstruction of the Small Intestine, Acta chir. Scandinav. **95**:519, 1947.

679. Crile, G., Jr.: Medical Aspects of Intestinal Obstruction, M. Clin. North America **32**:373, 1948.

680. Baumgartner, C. J.: Survey of Intestinal Obstruction, Arch. Surg. **55**:607 (Nov.) 1947.

681. Tendler, M. J.; Streeter, A. N., and Cartwright, R. S.: Acute Intestinal Obstruction, South. Surgeon **13**:551, 1947.

682. Skjold, A. C.: Bowel Obstruction, Minnesota Med. **31**:52, 1948.

683. Leiter, H. E., and Lyons, A. S.: Cecostomy for Prolonged Chronic Ileus, J. Mt. Sinai Hosp. **14**:934, 1948.

684. Laufman, H., and Method, H.: The Role of Vascular Spasm in Recovery of Strangulated Intestine, Surg., Gynec. & Obst. **85**:675, 1947.

685. Lichtenstein, M. E.: Tests for Determining the Viability of Strangulated Bowel, J. A. M. A. **135**:221 (Sept. 27) 1947.

Analysis of 336 cases, with particular reference to features suggesting the ultimate fate of strangulated bowel, indicated that the risk of subsequent gangrene increased with the length of the bowel involved.[686] Among 216 cases of replacement in which the color of the bowel was normal, the mortality was 9.7 per cent, as compared with 30 per cent in 20 cases in which the bowel was discolored. The presence of muscular contractions in the bowel and of pulsations in the mesenteric vessels was associated with a more favorable prognosis.

Intestinal Intubation.—Various improvements in the type of tube used and in the technic of intubation are described by Honor and Smathers[687] Kaslow[688] and Wild.[689]

Harris and Gordon[690] evaluate 100 intubations of the small bowel in 86 cases of distention or obstruction or both, utilizing a single lumen, mercury-weighted intestinal tube. This type of therapy was effective in 41 cases, without recourse to surgical intervention. In 59 instances, some type of operative procedure was performed as primary therapy. Complications included coiling of the tube in the stomach, failure of the tube to pass the pylorus, inability to withdraw the tube and rupture of the bag. The principal indication for intestinal intubation is distention of the small bowel, associated with simple adhesive obstructions or with certain medical conditions; it should never be used as primary treatment for strangulation of the small bowel or for obstruction of the colon. Herrera and his associates[691] state that the Harris tube possesses the advantages of easier passage through the pylorus, a larger single lumen and smaller total diameter. Cantor and his co-workers[692] state that the balloons of intestinal decompression tubes are permeable to gases, particularly carbon dioxide and hydrogen sulfide.

Berger and Achs[693] report a case in which perforation of the small intestine occurred after prolonged intubation; the patient recovered.

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686. Viability of Strangulated Bowel: Interim Report of Surgical Subcommittee of the Clinical Research Committee of the Public Health Department of the London County Council, Brit. M. J. **1**:43, 1948.

687. Honor, W. H., and Smathers, H. M.: A Double-Lumened Plastic Tube for Intestinal Intubation, Arch. Surg. **55**:498 (Oct.) 1947.

688. Kaslow, A. L.: A New Material and Tube Design in Gastrointestinal Intubation, Surgery **23**:293, 1948.

689. Wild, J. H.: The Stomach as a Cause of Difficulty in Intubating the Human Duodenum, Surgery **24**:70, 1948.

690. Harris, F. I., and Gordon, M.: Intestinal Intubation in Small Bowel Distension and Obstruction, Surg., Gynec. & Obst. **86**:647, 1948.

691. Herrera, R. E.; Millet, J. B., and Lawrence, G. H.: A Report on the Use of the Harris Tube, Surg., Gynec. & Obst. **85**:604, 1947.

692. Cantor, M. D.; Phelps, E. R., and Esling, R. H.: Effect of Intestinal Gases upon Balloons of Intestinal Decompression Tubes, Am. J. Surg. **75**:441, 1948.

693. Berger, L., and Achs, S.: Perforation of Small Intestine by Miller-Abbott Tube, Surgery **22**:648, 1947.

Intubation resulted in intussusception in 1 instance.[694] Brenizer[695] reports spontaneous coiling and knotting of a tube in the jejunum, proximal to an obstructing adhesion.

Redundant Postoperative Segments.—Black and McEachern[696] call attention to the potential hazards associated with the inverted end of the proximal segment of bowel, following division of the bowel and side to side anastomoses; they are dilatation, hypertrophy, ulceration and perforation. They are largely preventable by avoiding redundant segments of the proximal end.

Leakage from Enterostomy.—Strelinger[697] describes an appliance for preventing leakage from a gastrostomy or enterostomy wound.

Vascular Disease.—Cunningham[698] concludes that in malignant hypertension, severe vascular changes are noted in the gastrointestinal tract with great frequency (the site is second only to the kidney in incidence and severity), whereas in "benign" hypertension, severe arteriolar lesions are much less common. Periarteritis nodosa may be associated with ulcerative enteritis and perforation.[699]

Scleroderma.—Involvement of the jejunum and ileum is described.[700]

Mesenteric Thrombosis.—In a case in which massive resection was necessitated by mesenteric thrombosis, approximately 14 inches (36 cm.) of jejunum remained.[701] The patient survived, but poor fat digestion was evident, with frequent stools, a low serum cholesterol level and deficient absorption of calcium. Carbohydrate and proteins were well utilized. A similar case is described by Berman and others.[702]

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694. Warren, K. W., and Cattell, R. B.: Stenosis of the Intestine After Strangulated Hernia with Fatal Complication Following Intestinal Intubation, Am. J. Surg. **75**:729, 1948.

695. Brenizer, A. G., Jr.: Unusual Complication of Intestinal Intubation, New England J. Med. **238**:279, 1948.

696. Black, B. M., and McEachern, C. G.: Redundant Blind Segments of Intestine Following Side-To-Side Anastomosis with Division of the Bowel, Surg., Gynec. & Obst. **86**:177, 1948.

697. Strelinger, A.: An Appliance for Preventing Leakage of Gastrostomy and Enterostomy, Am. J. Digest. Dis. **15**:14, 1948.

698. Cunningham, G. J.: Intestinal Lesions in Malignant Hypertension, Brit. M. J. **1**:1075, 1948.

699. Berris, R. F.; Sawyer, K. C., and Lubchenco, A. E.: Periarteritis Nodosa with Ulcerative Enteritis and Perforation, Rocky Mountain M. J. **45**:394, 1948.

700. Brenner, A. J.: Scleroderma with Gastrointestinal Involvement, Rev. Gastroenterol. **14**:869, 1947.

701. Cogswell, H. D.: Massive Resection of the Small Intestine, Ann. Surg. **127**:377, 1948.

702. Berman, J. K.; Brown, H. M.; Foster, R. T., and Grisell, T. L.: Massive Resection of the Intestine, J. A. M. A. **135**:918 (Dec. 6) 1947.

Another instance occurred after resection of a carcinoma of the sigmoid.[703] The subject is reviewed by Debeyre.[704]

Perforation, Traumatic Resection and Foreign Bodies.—According to Sampson and Stauffer,[705] the term "subcutaneous rupture of the small intestine" designates a severance of the continuity of the bowel beneath an intact abdominal wall. Two cases are reported. Perforation of the jejunum may occur after apparently minor trauma.[706] Nine perforations of the jejunum and ileum were observed at autopsy in the case of a sailor exposed to the blast of an explosion.[707] Complete resection of a 12 inch (30 cm.) segment of ileum, without pentration of the abdominal wall, occurred in the case of a patient run over by a coal cart.[708] An unusual case of transection of the terminal ileum by an adhesive band is reported.[709] Obstruction of the small bowel had occurred approximately four months after appendectomy. Operation was performed eight days after the initial signs of obstruction, only a few hours after initial evidence of perforation of the bowel, but death ensued. In another case,[710] in which evisceration occurred subsequent to gastric resection, a jejunal fistula developed.

Snodgrass[711] reviews the subject of swallowed foreign bodies and presents interesting case reports. He concludes that foreign bodies generally cause little trouble unless arrested at one of the angles of the intestinal tract; the ileocecal region is the most common site of perforation. A patient was found to have a perforation of the ileum caused by a chicken bone, with inflammation and obstruction of bowel loops contained in a ventral hernia.[712]

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703. Saltzstein, H. C.: Mesenteric Thrombosis of Lower Ileum Following Resection of the Sigmoid Colon for Carcinoma, Am. J. Surg. **75**:854, 1948.

704. Debeyre, J.: Infarctus intestinal, Presse méd. **56**:424-D (June 16, supp.) 1948.

705. Sampson, D. A., and Stauffer, H. M.: Rupture of Small Intestine Complicating Injury of Pelvis, Radiology **49**:80, 1947.

706. Mortensen, J. D.: Perforation of Jejunum Due to Minor and Obscure Trauma, with Postoperative Escherichia Coli Peritonitis and Wound Infection Treated with Sulfathiazole and Streptomycin, Northwest Med. **46**:523, 1947.

707. Fink, H.: Intestinal Perforation Resulting from Atmospheric Blast, U. S. Nav. M. Bull. **47**:884, 1947.

708. Teng, P.: Complete Traumatic Resection of Ileum without Penetration of the Abdominal Wall, West J. Surg. **56**:viii, 1948.

709. Cameron, J. A.: Transection of Ileum by a Band, Canad. M. A. J. **57**:581, 1947.

710. Joseph, E. G.: High Intestinal Fistula and Its Treatment by the Use of a Pauls Tube, Am. J. Surg. **75**:640, 1948.

711. Snodgrass, T. J.: Foreign Bodies in the Intestinal Tract, Arch. Surg. **55**:441 (Oct.) 1947.

712. Kilbourne, B. C.: Perforation of Ileum by Ingested Chicken Bone Complicating Ventral Hernia, Ann. Surg. **127**:1226, 1948.

Benign and Malignant Tumors.—As reviewed by Root,[713] the most important roentgenologic signs of benign or malignant tumors are localized deformity, obliteration of the mucosal pattern, obstruction and ulceration.

Unusual cases include examples of diffuse polyposis,[714] intussusception produced by a pedunculated lipoma,[715] a large myoma producing intestinal obstruction by compressing the pelvic colon at the brim of the pelvis,[716] and a fibroleiomyoma.[717]

Hansen [718] states that hemangiomas are among the rarest of tumors of the small bowel, only 66 cases having been reported in the literature since 1860. Microscopically, hemangiomas fall into three types: (*a*) simple, consisting of newly formed capillaries; (*b*) cavernous, consisting of large, blood-filled spaces, and (*c*) combined, a combination of the first two. Grossly, the tumors fall into four classes: (1) multiple phlebectasia; (2) cavernous hemangioma; (3) simple capillary hemangioma, and (4) localized angiomatosis. The symptoms may be those of hemorrhage and obstruction. Associated angiomas of the skin may be present. Cavernous hemangiomas may contain phleboliths demonstrable by roentgenologic examination.

A neurinoma, the size of a man's head,[719] and a neurofibrosarcoma, in a patient with neurofibromatosis (von Recklinghausen's disease),[720] are reported.

Of 62 tumors of the small bowel, 44 were benign.[721] Two of these caused symptoms because of intussusception. Twelve neoplasms were found to be carcinomas. The chief symptoms in the cases of malignant growths were abdominal pain, vomiting, melena, diarrhea and weakness. The tumors were palpable in 9 cases. A lesion of the small bowel

713. Root, J. C.: Roentgenologic Diagnosis of Tumors of the Small Intestine, M. Clin. North America **32**:436, 1948.

714. Manfredi, F. J., and Vivoli, D.: Poliposis difusa o generalizada del intestino delgado, Rev. Asoc. méd. argent. **61**:632, 1947.

715. Sherry, L. B.: Lipoma of the Ileum Causing Ileo-Ileal Intussusception in an Adult, West. J. Surg. **55**:604, 1947. Lawler, R. H.; Ragins, A. B., and Silverstein, J.: Submucous Lipofibroma of the Ileum, Am. J. Surg. **74**:820, 1947.

716. Cookson, C. C.: Myoma of the Small Intestine Causing Intestinal Obstruction, Lancet **2**:280, 1947.

717. Froelich, A., and Gepts, W.: Fibroleiomyome du jejunum, Acta gastroenterol. belg. **10**:515, 1947.

718. Hansen, P. S.: Hemangioma of the Small Intestine, Am. J. Clin. Path. **18**:14, 1948.

719. Möller, W.: Solitary Neurinoma of the Small Intestine, Acta chir. Scandinav. **96**:1, 1947.

720. Clay, A. G. H.: Neurofibrosarcoma of the Small Intestine Associated with Von Recklinghausen's Disease, Post-Grad. M. J. **23**:572, 1947.

721. Dundon, C. C.: Primary Tumors of the Small Intestine, Am. J. Roentgenol. **59**:492, 1948.

was demonstrated in 8 of 11 cases in which roentgenologic examination was made. The average duration of life in 12 cases in which operation was performed was eight and one-half months. In 5 cases, a typical history was not given, the lesion caused no obstruction or bleeding, and no abdominal mass could be palpated. Among 52 cases of malignant tumors of the small intestine,[722] there were 21 carcinomas of the duodenum and 1 lymphosarcoma; 17 per cent of these tumors were in the supra-ampullary portion, 61 per cent in the periampullary portion and 22 per cent in the infra-ampullary portion.

Weinbaum[723] reviews 14 cases of primary malignant tumors, including 4 adenocarcinomas of the duodenum, 1 of the jejunum, 1 leiomyosarcoma of the jejunum, 1 lymphocytic lymphoma of the jeunum, 1 carcinoma of the jejunoileal junction, 3 carcinomas of the ileum, 2 carcinoids of the ileum and 1 reticulum cell lymphoblastoma of the ileum. Of 19 cases of tumors described by Eckel,[724] 7 lesions were benign and 12, malignant. Additional cases are reported by Delano[725] and Lippert.[726] Carcinoids and similar tumors are described by several other authors.[727]

Rabinovitch and others[728] report 9 cases of sarcoma of the small bowel, in 5 of which the lesion was in the colon and in 1 in the rectum. The diagnosis was not made before operation, and in many cases not until the histologic examination. Other interesting cases are described.[729]

(To Be Continued)

722. Doub, H. P.: Malignant Tumors of the Small Intestine, Radiology **49**: 441, 1947.

723. Weinbaum, J. A.: Primary Malignant Tumors of the Small Intestine, Rev. Gastroenterol. **14**:478, 1947.

724. Eckel, J. H.: Primary Tumors of the Jejunum and Ileum, Surgery **23**:467, 1948.

725. Delano, P.: Tumors of the Small Intestine, Am. J. Roentgenol. **59**:685, 1948.

726. Lippert, R. M.; Potozky, H., and Nelson, L. E.: Carcinoma of the Terminal Ileum: A Cancer Study, J. South Carolina M. A. **44**:123, 1948.

727. D'Albora, J. B., and Ingegno, A. P.: Carcinoid Tumors of the Small Bowel, Gastroenterology **10**:310, 1948. Fraenkel, G. J.: Carcinoid Causing Obstruction, Lancet **1**:404, 1948. Hoffman, J. M.: Tumor Intussusception, Northwest. Med. **46**:950, 1947.

728. Rabinovitch, J.; Grayzel, D. M.; Sawyer, A. J., and Pines, B.: Sarcomas of the Small and Large Intestine, Surg., Gynec. & Obst. **85**:333, 1947.

729. Salvesen, H. A.: Symptomatic Sprue Due to Reticulosarcomatosis of the Small Intestine and the Mesentery Glands, Gastroenterologia **73**:166, 1948. Carnes, E. H.: Reticulum Cell Sarcoma of the Ileum, Am. J. Surg. **74**:49, 1947. Bastrup-Madsen, P.: Plasmocytoma of Small Intestine, Nord. med. **35**:1919, 1947. Dónovan, R. E.: Invagination cronica de intestino, por sarcoma fibroblastico (2 casos), Bol. y trab., Acad. argent. de cir. **31**:607, 1947. Badia, P. D.: Primary Hodgkins Sarcoma of the Jejunum with Perforation: Resection and Radiotherapy, Am. J. Surg. **59**:577, 1947.

News and Comment

GENERAL NEWS

Postgraduate Courses at University of California.—The University of California Medical School, San Francisco, will hold a postgraduate course on physics in radiation therapy, September 6 through September 9. The course will consist of ten lectures by Dr. Edith H. Quimby, Associate Professor of Radiology, Columbia University, on physics as it pertains to ionizing radiations. Emphasis will be placed on the basic principles and their application to problems of therapy. The course will be of particular interest to radiologists, dermatologists and gynecologists.

The University of California has also scheduled a course in the medical aspects of nuclear energy, to be given from August 29 through September 3. Subjects to be discussed include fission and the chain reaction; the pile and the bomb; principles and applications of radioactive tracers to the medical and biologic sciences; diagnostic applications of artificial radioactivity; treatment of leukemias and allied conditions with radiophosphorus; radioiodine in the treatment of hyperthyroidism and carcinoma of the thyroid; diagnosis and treatment of acute and chronic radiation illnesses; problems of protection associated with the handling of radioactive materials; radiologic hazards associated with large scale release of nuclear energy; evaluation of biologic experiments conducted at Bikini, and genetic effects of ionizing radiation.

Detailed printed programs for these courses may be secured from Dr. Stacy R. Mettier, Professor of Medicine, Head of Postgraduate Instruction, Medical Extension, University of California Medical Center, San Francisco 22.

Revised Edition of Motion Picture Reviews Now Available.—The Committee on Medical Motion Pictures has completed the first revised edition of the booklet entitled "Reviews of Medical Motion Pictures." It now contains all the film reviews published in *The Journal of the American Medical Association* to Jan. 1, 1949. It also includes a classified table of contents and list of motion pictures available through the Motion Picture Library, American Medical Association.

The purpose of the reviews is to provide a brief description and evaluation of motion pictures which are available to the medical profession. Each film is reviewed and commented on by competent authorities.

Copies are available on request from: Committee on Medical Motion Pictures, American Medical Association, 535 North Dearborn Street, Chicago 10, Illinois.

Annual Meeting of Mississippi Valley Medical Society.—The fourteenth annual meeting of the Mississippi Valley Medical Society will be held at the Jefferson Hotel, St. Louis, September 28, 29 and 30, under the presidency of Alphonse McMahon, M.D. The entire program, including some sixty scientific and technical exhibits, is planned to appeal to the general practitioner. No registration fee will be charged. During the course of the meeting, on September 28 and 30, respectively, the American Medical Writers' Association, formerly the Mississippi Valley Medical Editors' Association, and the Missouri chapter of the American Academy of General Practice will hold their annual meetings at the same hotel. Programs of all three meetings may be obtained from Harold Swanberg, M.D., 209-224 W. C. U. Building, Quincy, Ill.

School of Medical Illustration.—The first school of medical illustration in the southeastern United States has been opened at the University of Georgia School of Medicine.

The courses are designed to equip illustrators for work in all fields of scientific illustration. Since a knowledge of the technics of medical illustration is necessary for the production of exemplary illustrations in various fields of scientific education and publication, special students who wish to apply such technics to a field of classical study other than medicine may be accepted.

Only a limited number of applicants are selected each year for the training. Applications for admission may be addressed to the Registrar, University of Georgia School of Medicine, Augusta, Ga.

Convention of Biological Photographic Association.—The nineteenth annual meeting of the Biological Photographic Association, Inc., will be held in Cleveland, September 7 through September 10. The Pre-Convention issue of the *Biological Photographic Association Journal* will include hotel reservation cards as well as more complete details of the convention plans. Entry blanks for the salon may be obtained from Mr. William Stevenson, Mt. Sinai Hospital, 1800 East 105th Street, Cleveland 6. Other information concerning the convention may be secured from its general chairman, Mr. David Lubin, 130 Keats Lane, Berea, O.

Postgraduate Course in Psychiatry and Neurology.—A full time postgraduate course of twelve weeks in psychiatry and neurology will be offered at the Langley Porter Clinic, University of California Medical School, San Francisco, August 29 through November 18. The course will be under the chairmanship of Karl M. Bowman, M.D., Professor of Psychiatry, University of California. The fee will be $200. Program and information may be obtained from Stacy R. Mettier, M.D., Head of Postgraduate Instruction, Medical Extension, University of California Medical Center, San Francisco 22.

Japanese Medical Journal.—The *Japanese Medical Journal,* official organ of the National Institute of Health of Japan, has been recently released. Volume 1, number 1 appeared in February 1948. The magazine is published bimonthly.

The managing editor of the new journal is Hidetake Yaoi. Editorial offices are located at Shiba Shirokane Daimachi, Minato-Ku, Tokyo.

All articles appearing in the February 1948 and April 1948 issues are by Japanese authors and appear in English.

Book Reviews

Twentieth Century Speech and Voice Correction. Edited by Emil Froeschels, M.D. Price, $6. New York: Philosophical Library, Inc., 1948.

This volume of twenty-two chapters is a series of essays concerning the various phases of corrective speech training organized for professionals and others interested in remedial measures.

Emil Froeschels, a leader in speech and voice therapy, organized the volume and contributed three of its chapters. Two other chapters are written by physicians. These five chapters deal with the anatomy, physiology and pathology involved in speech and in speech defects. They also describe surgical measures to correct congenital and traumatic lesions. The remaining seventeen chapters are written by sixteen professional speech and voice teachers, trainers and correctionists. The volume is not concerned with training the normal voice but with remedying marked defects.

Considerable space is devoted to aphasia, aphonia, dysphonia and related subjects, with full discussion of their neurogenic background. In line with this, considerable space is devoted to the development and training of the residual ability to hear certain tones present in the great majority of those considered to be totally deaf. The psychologic aspects of these problems are thoroughly discussed as well as the underlying anatomy and physiology.

One chapter is concerned with training the speaking voice and one with training the singing voice. However, the major emphasis of the volume is concerned with the correction of major defects of speech and with teaching those to speak who have never spoken or who have lost the ability to speak. The final chapter is on voice training after total laryngectomy.

Tuberculosis in Childhood. Second edition. Revised by Henry F. Macauley. Price, $7. Pp. 228. Baltimore: Williams & Wilkins Company, 1948.

This book can be recommended to the pediatrician and the general practitioner as a good over-all picture of tuberculosis in childhood in all its phases. The successful treatment of tuberculous meningitis with streptomycin deserves more attention in a book appearing in 1948 than the mere statement that the drug shows some promise. The advantage of BCG vaccination of tuberculin-negative young adults as well as the importance of immediate treatment of primary tuberculosis in this age period is particularly emphasized.

Investigations into the Development of the Pituitary and Hereditary Anterior Pituitary Dwarfism in Mice. By Torben Francis. Copenhagen: Ejnar Munksgaards Forlag, 1944.

This monograph by Torben Francis has been translated from the Danish. Its object is to study the development of the adenohypophysis in mice with hereditary anterior pituitary dwarfism. The work of other investigators of the anterior pituitary lobe in the experimental animal and in the human being is reviewed in detail.

In 1929 Snell found dwarfism in a strain of mice. This strain has been studied extensively, particularly with reference to the pituitary gland. Two hundred

fetuses and young of this strain of mice constitute the material for the experimental study. They were killed after the age of 9 fetal days, by which time the anlage of the anterior pituitary lobe is developed, to the age of 12 days after birth, when the dwarf growth manifests itself. In addition, the pituitary glands of older mice which were dwarfs and some which were normal were studied. All the histologic observations on fetuses, immature mice, dwarfs and nondwarfs of the dwarf strain have been compared with those on mice from a strain which has no hereditary disposition to dwarfism.

The technic required to secure the fetuses from the uterus, the method of measurement and the excision and embedding of the pituitary gland are discussed in detail.

The histology and embryology of the adenohypophysis and other endocrine glands of the dwarf mouse from the ninth fetal day to maturity are discussed in great detail. The role played by the different types of cells in the growth of the body is presented clearly, which is a real contribution to the understanding of dwarfism.

This monograph is based on a thorough review of the literature on the anterior pituitary lobe and an extensive embryologic and histologic study of the pituitary of the strain of dwarf mice. The presentation of the material lacks organization and makes the reading difficult. One has the feeling that the author tried too hard to achieve completeness and in so doing sacrificed clarity, which will result in the book's being read less than it should by those who are interested in knowing more of this important and interesting structure of the body.

Pathology. Edited by W. A. D. Anderson, M.D. Price, $15. Pp. 1,453, with 1,183 illustrations. St. Louis: The C. V. Mosby Company, 1948.

This is an excellent new textbook of pathology written by Dr. W. A. D. Anderson and thirty-one distinguished collaborators. The organization of the text is conventional. However, the constant emphasis in relating the postmortem findings to antemortem clinical findings and disturbances of function makes the book of more interest than older ones. The effects of radiation and chemical injury; viral, fungus, protozoal and helminthic infections; diseases of the skin, and diseases of the skeletal system receive relatively more attention than in most books on pathology. The extensive bibliographies will be appreciated by graduate students and practitioners. The book has everything required to make it eminently satisfactory for both student and physician. It deserves a wide distribution.

Practical Aspects of Thyroid Disease. By George Crile Jr., M.D., F.A.C.S. Price, $6. Pp. 355, with 101 illustrations. Philadelphia: W. B. Saunders Company, 1949.

This book is especially valuable because it brings the reader up to date on accepted opinions on diseases of the thyroid gland. The author has avoided long discussions, charts and experimental data and, with a minimum of words, has covered each subject well.

The chapters on basic physiology and pathology clearly explain today's concept of these subjects. Toxic diffuse goiter and toxic nodular goiter are well distinguished with regard to diagnosis and treatment. In many minds, there is confusion regarding the indications for the use of iodine, antithyroid drugs and thyrotropic hormone and for surgical intervention; these are clearly explained and differentiated. The chapter on the use of antithyroid drugs is especially well organized and written.

Four chapters are devoted to the discussion of malignant tumors of the thyroid. The author uses the accepted classification of the common carcinomas of the thyroid, dividing them into papillary and nonpapillary types, and discusses differentially the symptoms, pathologic features and treatment.

The chapter on roentgen therapy and the use of radioactive iodine is primarily a summary of the opinions of other workers in this field and of results of their experiments, together with observations from the author's limited experience. It confirms a conviction that that avenue of therapy, while most fascinating, still must be left to well organized and controlled clinics for further development.

The book is made complete by inclusion of discussions on the symptoms and diagnosis of hyperthyroidism, the technic of thyroidectomy, anesthesia, preoperative and postoperative care, complications, inflammatory conditions and extrathyroid diseases. The reviewer knows of no other single volume which covers the whole subject of thyroid disease so clearly, yet briefly, as does this book.

Thyroid Enlargement and Other Changes Related to the Mineral Content of Drinking Water (with a Note on Goiter Prophylaxis). By Margaret M. Murray, J. A. Ryle, Beatrice W. Simpson and Dagmar C. Wilson. Medical Research Council Memorandum no. 18. Price, 9d. Pp. 39. London: His Majesty's Stationery Office, 1948.

This booklet brings out most of the well known facts about endemic goiter, particularly regarding its etiology and treatment. It reports a survey of adolescents and young adults in counties and towns in various parts of England and Scotland, and of the drinking waters in the same communities, to determine their iodine content and "hardness"; findings are correlated with the incidence of endemic goiter.

The authors note that McClendon and Williams, in the United States, found those areas in which the drinking water contained 3 mg. or more of iodine per liter to be practically free from goiter. By comparison, in England generally it was found that an iodine content of 5 mg. of iodine per liter was the preventive level; this is attributed to the "hardness" of the water. In those regions of England and Scotland where the water was "soft," a level of 3 mg. of iodine per liter prevented goiter, as in the United States.

It had previously been observed that a high incidence of goiter existed in those regions where an excess of fluorine was present in the drinking water. Admitting that the problem is complex, the observers state the belief that goiter was absent or minimal in those regions whenever the iodine intake was adequate.

The minimal daily requirement of iodine has never been definitely established, but it is the feeling of these writers as well as of others that even in those regions having water of high iodine content, that source must be supplemented by iodine in the diet to meet minimal requirements.

A parallel is drawn between the incidence of cretinism and deaf-mutism and that of goiter in areas where a deficiency of iodine exists.

Several charts are published which compare the incidence of goiter with the iodine content and the "hardness" of available drinking water in specific counties in England and Scotland, which should be valuable to physicians and health officers.

The authors postulate and fairly convincingly show that the primary cause of endemic goiter is the deficiency of iodine in the available supply of water and foods. They advocate the addition of iodine, in the form of iodized salt, to the diet as the prophylactic treatment.

A History of the Heart and the Circulation. By Frederick A. Willius, M.D., and Thomas J. Dry, M.A., M.B., Ch.B., M.S. in Med. Price, $8. Pp. 473, with 160 illustrations. Cloth. Philadelphia and London: W. B. Saunders Company, 1948.

This book deals with the sources from which knowledge of the heart and vascular system arises. It is divided into three main sections. The first section consists of a résumé of the chronologic presentation of this subject from 5000 B.C. to 1925 A.D. As this section occupies 225 pages one must realize that it is packed with information. The section mentions the name of the contributor, the subject of his contribution and the date on which the contribution was made. The story progresses rapidly from era to era but contains information about practically everyone who made an important contribution to this subject. A good list of references follows each chapter in this section.

The second section is made up of a series of special biographies. These are short sketches of the lives of the men who the authors believe deserve special mention. The sketches are well done, but this section is sure to provoke some criticism and perhaps a little resentment. The authors have attempted to disarm this criticism in their preface by suggesting that their selection of subjects for the special biographies might not be in agreement with the selection of others. They point out that the achievement of unanimity in this selection would be impossible. This is true. It would seem that the group might well have been discussed in the running account (as indeed they were, briefly) and thus criticism would be avoided. This reviewer wonders at the omission of Vaquez, Heberden, Herrick and Maude Abbott from the list, to mention but a few. There are twenty of these special biographies. They start with Hippocrates and end with Sir Thomas Lewis. Rudolph Matas is the only survivor in the group. Again, a list of references follows each biographic sketch.

The third section is written in outline form and contains a chronologic account of subject matter. Anatomy of the heart and circulation is dealt with chronologically and then aneurysm and related subjects. This is well done.

The book contains no mention of the later surgical operations for heart disease or of the subject of angiocardiography. It is assumed that the authors considered that these subjects were to be discussed as the developments of a later period.

It is noteworthy that so many fundamental contributions to the subject were made by persons who today would not be called "cardiologists." The contributions of physicists, surgeons, physiologists and pediatricians abound. Neurologists are included. Among the internists, a great number were, and considered themselves, general internists and not "cardiologists." Rokitansky and Bright, for instance, achieved greater fame in fields other than that of heart disease. One wonders about the advisability of too sharply limiting a special field of endeavor in medicine.

The authors in the preface point out the possibility of errors' creeping into such a comprehensive work. This is particularly true in the matter of credit. The authors assume that the contribution is always of greater importance than the man who made it. This is true, but the matter of credit is always of importance to the man or to his community or even to his country. For instance, the authors credit C. J. B. Williams, of Great Britain, with the first report of a successful closure of a stab wound of the heart. The credit for this usually goes to a different Williams—Dan Williams, an exceedingly fine Negro surgeon, of Chicago. However, controversial works are always exceedingly interesting and instructive, and this is no exception.

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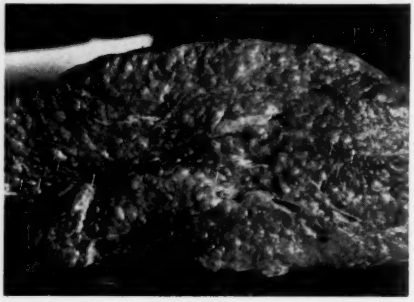

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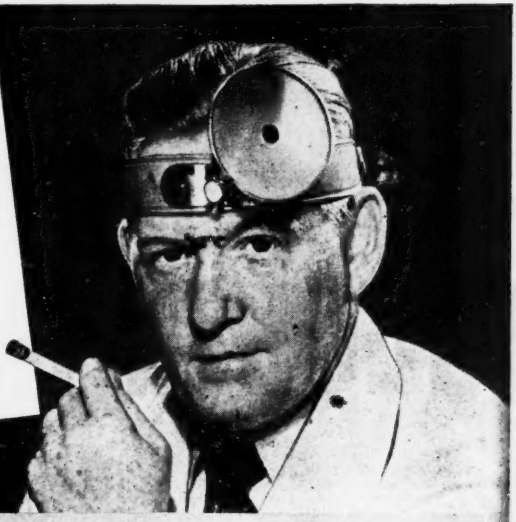

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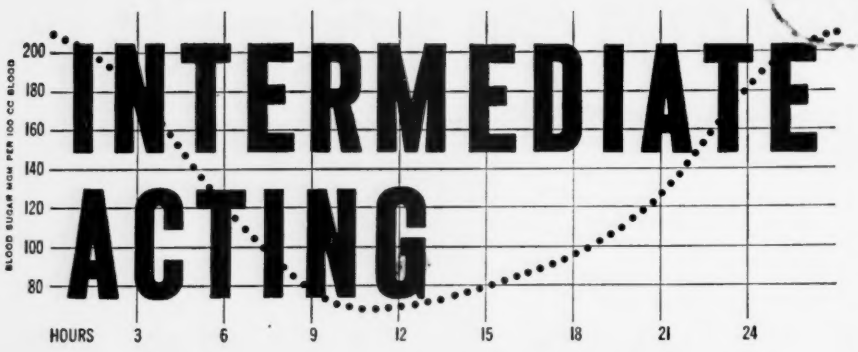

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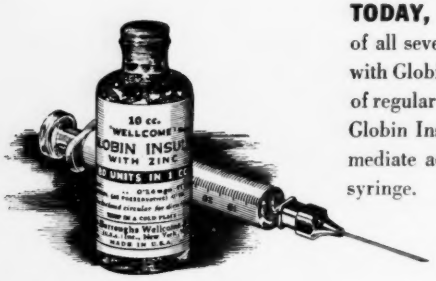

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1. Rohr, J.H., and Colwell, A.R.: Arch. Int. Med. 82:54, 1948.
2. ibid Proc. Am. Diabetes Assn. 8:37, 1948

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